National Institutes of Health

Research Plan

December 1980

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service
National Institutes
of Health

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH

TO : The Assistant Secretary for Health and Surgeon General
Through: ES/PHS _____

DATE: December 22, 1980

FROM : Director, NIH

SUBJECT: NIH Research Plan, Fiscal Years 1982-84

Enclosed for your review is the NIH Research Plan for Fiscal Years 1982-84. FY 1981 figures shown are those contained in the current continuing resolution. Budget figures for FY '82 and projections for FYs '83 and '84 are excluded from the document. Over the past four years the planning process at NIH has evolved into a structured set of meetings of the NIH Director with the Institute Directors to enhance and integrate planning, budgeting, and legislative activities in anticipation of appropriations committee hearings and the development of the Department budget for the next two years. This research plan is the result of planning activities during the past year. These have concentrated on examining ways to stabilize support for research project grants, on involving a broader segment of the community in the NIH planning process, and on continuing to press ahead with the effort to develop a strategy and plan for support of the Department's health research activities.

The main challenge facing NIH today is to sustain the capacity and effectiveness of the present research system, which has just experienced two decades of rapid growth, followed by a leveling off period and entry into a phase of high inflation and deepening austerity. The quest to maintain scientific productivity and to avoid excessive strain on the present enterprise in an era of economic difficulty will require skill and ingenuity. It will present the NIH with an array of specific problems in the areas of legislation, management, staffing, and budgeting.

The pages which follow address three overriding issues. In addition to the importance of sustaining system capabilities (already noted above) is the need to (1) manage a series of health research matters that extend beyond the traditional responsibilities of NIH, and (2) to examine the problems involved in the public review and accountability of research.

This plan presents an overview of NIH strategy in terms of the SATT approach (Science Base, Applications, Technology Transfer, and Training). Through planning exercises the NIH has refined this model for classifying and describing the allocation of NIH resources by major purpose. Each Institute is reviewed individually in a chapter which includes a Director's overview, an outline of planned program changes for FY 1981-82, and a summary of the review sessions of that Institute with the Director, NIH. The appendices include the guidances for review sessions, testimony of the NIH Director before the House and Senate Appropriations Committee based on those sessions, and the December 1979 proceedings of the Advisory Committee to the Director,

NIH, that examines the stabilization initiatives and its implications for the rest of the NIH programs.

Dr. Joseph G. Perpich, Associate Director for Program Planning and Evaluation, has overall responsibility for the planning process. Dr. Solomon Schneyer, Mr. Kurt Habel, and the DPA planning staff are responsible for the development of the NIH research plan. At Dr. Perpich's request, a committee of Institute planning and evaluation officers recently assessed NIH program review sessions to develop recommendations for structural improvement. The recommendations, which are now being implemented, provide for two separate individual review sessions, with the first series toward the end of the year devoted to planning, budgeting, and legislative activities, and a second series, in the spring, concerned with specific programs and policies. This coming spring the reviews will examine, among other matters, NIH and academic relationships with the industry sector. Included in the appendix is a report of the Planning and Evaluation Officer's Report and summary minutes from the Office of the Director's staff and Institute Director's meetings devoted to a review of the Report.

The planning/appropriations review sessions in December are focusing on a request contained in the Health Appropriations Committee report for FY 1981. This request specified that NIH should carefully consider the impact of stabilizing research project grants (approximately one-half of the NIH budget) on the rest of NIH program plans and priorities for FY 1982 and 1983. Elements to consider include the intramural program, research and resources centers, training, and applications and technology transfer. Those HHS health research initiatives for which NIH is the sponsoring agency will also be reviewed.

Looking beyond the planning process itself to the future of NIH as a whole, it is clear that if economic constraints on the size of the health research system cannot be relieved, then there must be shifts of resources from one field to another of research and research training, in concordance with changing research needs and opportunities. It will continue to be necessary to maintain a proper balance between fundamental inquiries and practical application, and to set research priorities without departing from the primary requirement of scientific quality.

The proceedings of the Advisory Committee to the Director, NIH, are included as a supplement to the research plan. As an adjunct to the NIH planning effort, the Committee has been examining a number of cost and accountability issues as these affect the academic science sector. The urgency of these issues has grown in recent years as a consequence of the impact of inflation on research costs and available institutional resources, the leveling off of Federal funds for research, and the recent major revision of cost and accounting guidelines for Federal support of research in academic settings. In aggregate, these problems seriously disturb the tenor of the long and fruitful partnership between the Government and the universities.

At its meeting in May 1980 the Committee examined NIH-supported research costs--both direct and indirect--associated with that support. At its October 20-21 meeting, it examined several possible alternatives for research funding which might reduce some of the tension in the existing relationship.

One option involved some modification of several policy and process features in the existing NIH grant system. The second would make greater use of flexible awards to institutions, along lines of the general research support grants and the comprehensive institutional grant awarded in the past to the Sloan-Kettering Memorial Cancer Center. The third and most discussed was the proposal for a new mechanism of support, a "fixed obligation grant."

In all of the Committee discussions, there has been full participation by the Department and PHS: indeed, the HHS Inspector General Designate has given special attention to the need to create a government/university open forum in which to consider a wide range of cost and accountability issues. Thus, the record of Committee proceedings is included as a supplement to the NIH Plan, for the insights it provides on policy issues.

Copies of the NIH Plan and the HHS Planning Document will be sent to all who participated in the development of the HHS health research planning effort.

D S Fredrickson

Donald S. Fredrickson, M.D.

NATIONAL INSTITUTES OF HEALTH
RESEARCH PLAN

FISCAL YEARS 1982-1984

December 1980

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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service National Institutes of Health

FOREWORD

This Research Plan, the second in a series, is an outgrowth of newly enhanced planning and evaluation processes at the National Institutes of Health. Formal planning activities began in the 1960s with added requirements for documentation around 1970. Research Plans have been developed since then, but none of these has derived from the kind of processes that characterize planning efforts for FY 1980-82, 1981-83, and 1982-84.

Perspective on current planning processes is afforded by briefly reviewing the nature of earlier planning efforts and the specific problems which confronted NIH planning.

The Research Plan for 1977-81. This plan contained the NIH budget proposal, the Institute programs, issue papers, and a legislative plan. (In previous years lengthly versions of the Institute programs and legislative plans were in separate volumes.) The range of issues dealt with was broader than previously, and a number of issue papers were included relating both to the substance of the NIH mission and to the management of biomedical research. The interface between NIH knowledge development and other components of the health enterprise was also examined.

The Research Plan for 1978-82. This Plan provided a fuller discussion of plans and opportunities for research progress than formerly. It was formulated during an evolutionary period for NIH. Extensive public review of various aspects of NIH programs had been under way by the President's Biomedical Research Panel, a high level group broadly charged to review, assess, and make recommendations with respect to policy aspects of NIH research programs. The Panel's conclusion was contained in a report submitted to the President and to the Congress. Conceptual distinctions between the basic, applied, and developmental elements of NIH activities were emphasized in this Plan. (The definitions are essentially those employed by the National Science Foundation.)

The Research Plan for 1979-83. This Plan reflected the development of a more carefully structured long-range planning process. The major elements included strengthening of the processes for interaction and decision-making between the NIH Director and the individual NIH Institute Directors and their respective senior staffs, as well as improved integration of the planning, financial, and legislative functions, which is reflected in all subsequent Plans. The planning cycle began for the first time in September (instead of February), when the Departmental guidances are usually transmitted to the agencies. This spread the NIH planning process over eight months--a much more manageable period than the two or three months afforded in previous years.

The 1979-83 Plan addresses the entire health research continuum from knowledge development to diffusion of research results. The key focus in the Plan was the evaluation of medical applications. The traditional tool for the

evaluation of results of most clinical research before they are generally introduced into the health care system is the clinical trial, designed to assess the effect and value of prophylactic, diagnostic, and therapeutic agents, devices, regimens, and procedures on human subjects. A Clinical Trials Committee, established earlier, had defined criteria and provided guidance as to which clinical trials ought to be supported. The emphasis now turned to ways to achieve consensus on those research results deemed ready to be generally adopted into health care practice. Much effort was addressed to NIH responsibilities in this connection.

In the 1979-83 Plan, considerable attention was also devoted to trans-NIH health problems: how to transcend a specifically disease-oriented organizational structure in developing a fully coordinated approach to such disease as diabetes and to fundamental cross-cutting disciplines such as genetics or epidemiology. NIH began aggressively to identify these problems and to develop oversight mechanisms appropriate to each. Thus, six trans-NIH health areas were identified in the 1979-83 Plan--arthritis, diabetes, cystic fibrosis, epidemiology, genetics, and nutrition.

Finally, the emphasis on shaping a responsive research policy was highlighted, especially the NIH lead role in the development of the recombinant DNA research guidelines. These efforts have resulted in the formation of review boards to oversee human experimentation, animal care, and recombinant DNA experiments in the interests of public safety.

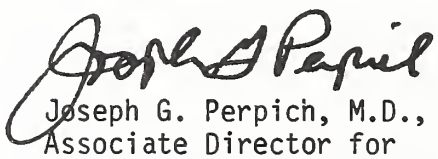
The Research Plan for 1980-82. The NIH Research Plan for 1980-82, published in April 1978, reflects a continuing evolution of the planning process and of substantive issues. The planning process was begun earlier and provided with more structure. One important innovation was the development of a new approach to characterize NIH activities. A classification system was devised to address and characterize the research continuum. This derived in particular from a high administration priority for basic research. The SATT approach--Science Base, Applications, Technology Transfer, and Training--was adopted, and the review of Institute research programs was conducted within the context of this new approach. Thus a common framework was provided within which activities and issues could be viewed as they occur in the sequence of knowledge development--a structure around which the general flow and direction of NIH activities could be assessed.

The Research Plan for 1981-83. The Plan responds in part to the challenge posed by former HEW Secretary Califano to develop health research principles and a five-year plan for health research activities in the Department. A major focus was the stabilization of the Science Base--principally investigator-initiated research project grants. The thrust of the reviews embodied in this Plan is the allocation of monetary resources of each of the Institutes according to the four SATT categories.

Thus, the NIH Research Plan has increasingly become an integral part of the formulation and conduct of research programs. The planning function helps to establish the framework through which goals, objectives, and research strategies are assessed, research priorities set, resource allocations made, new programs developed and implemented, and existing programs modified.

The Advisory Committee to the Director, NIH, serves as an important public policy forum for research planning, legislative, evaluation, and budgetary issues. The proceedings of the Advisory Committee have appeared in many of the documentary materials published by this Office vis-a-vis the HHS health research planning efforts and the revision of NIH guidelines for recombinant DNA research. The Committee has assumed a lead role in the broad area of government/university relationships. Thus, the proceedings of the Committee now appear as a supplement to the NIH Research Plan.

Much has been done, but much more remains to be done to integrate planning, budget, evaluation, and legislation at NIH and with related processes in the Department and the Federal Government. Continuing attention to such "process" issues will permit more constructive interaction among policy makers concerned with advancing the health sciences. Implementation of recommendations contained in the Planning and Evaluation Officers Committee Report that appears in the appendix to the Research Plan should further advance this process.



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DIRECTOR'S PREFACE

Planning activities at the NIH during the past year have concentrated on examining approaches to stabilizing research project grants, to the balance between such support and all other instruments for scientific inquiry, on ways of involving a broader segment of the community in the NIH planning process, and on continuation of the initiative to develop a five-year plan for health research activities in the Department. These activities have been taking place during a time when national resources are not sufficient to meet all competing concerns. The problem in planning health research in general and biomedical research in particular is how best to sustain the high level of performance of the enterprise in the face of serious budget constraints.

Stabilization Initiative

New directions in funding have been established in the last five years at the NIH. The share of NIH research dollars going to project grants has risen. Support for centers, clinical trials, and development by contracts has proportionately declined. The decision to seek a general commitment on the part of both the Administration and the Congress to strive for a floor of about 5,000 competing project grants to be funded annually (implying a total of about 16,000 active grants per year) was a bid for long-term stability of the single most important mechanism for supporting fundamental research. This initiative grew out of the National Conference on HHS Health Research Principles where representatives from the health research community strongly emphasized the need to provide steady support in the search for fundamental knowledge, from subsequent planning efforts designed to translate the broad principles articulated by the Conference into program actions, and from Congressional interest in introducing a greater degree of predictability into the support of basic research. This initiative has now been adopted by both the Administration and Congress for FY 1981.

A project grant is a commitment of support for a period of several years. Each year these commitments are met first; applicants for renewal of their grants join those submitting new proposals in competing for the residual of the total funds allotted for project grants. The number of grants awarded each year thus depends heavily upon the annual appropriation, and can not be reliably predicted in advance. It is subject to considerable variation. The total number of grants in the portfolio of a given Institute reflects several cumulative years of funding. Throughout the seventies, the number of "new and competing" awards made each year showed a vacillating course. The bottom (2,590) was touched in 1973. The number awarded rose sharply for the next two years (4,500 and 4,600), fell badly again in 1976 (3,460), and then rose dramatically in 1978 (5,200) and 1979 (5,900). The stabilization initiative should smooth out these perturbations and introduce a quantum of predictability into this major, important form of NIH support.

But, the implementation of this initiative in 1981 will bring with it several problems that must be addressed as part of future steps. Within existing constraints on the total budget level, this approach will place strict limits on the amount available for other activities, notably research training, R&D contracts, centers, and intramural research. If this initial emphasis is continued arbitrarily, the long-term result will be to distort resource distribution in NIH programs to the detriment of the science base as a whole. The various mechanisms for supporting science base activities all contribute in important ways. Thus, research centers and resources enrich the research environment and provide unique opportunities for interdisciplinary collaboration; indeed, without the resources which they provide many individual investigators would not be able to function. Research contracts permit the agencies to stimulate research in needed areas and to manage and coordinate complex undertakings such as clinical trials; and the intramural research programs provide a stimulating, stable environment for high-quality, often high-risk or long-range investigations, as well as a resource for the national and international research communities. The next step, then, is to restore and strengthen the equilibrium of the science base.

Subsequent analysis and discussion of this initiative has highlighted the interdependency of the scientific discovery process and the maintenance of a pool of well-trained investigators. There is a close and reciprocal relationship between the continued productivity of research and the availability and replenishment of the supply of investigators. The reciprocal nature of the relationship is clearly understood. The ability to conduct research is wholly dependent upon the availability of well-trained investigators. We know, for example, that individuals with NRSA predoctoral support complete their training in less time than those who do not have this support and it is our belief that the training is more effective. We can also predict that post-doctoral research training will increase the likelihood of subsequent successful participation in biomedical research. The training programs also provide the premier opportunity for the research agencies to maintain and strengthen the institutional training environment so that the numbers and kinds of investigators being trained will be prepared to conduct research in areas of national need. There has been a steady erosion over the last eight years in the number of research trainees supported by NIH. Recently the decision to stabilize research project grants required cutbacks in research training. There is substantial consensus that some restoration of resources and long-term predictability for research training are essential to the health of the research enterprise. This, then, would represent the second step in this initiative.

Broadening the Planning Process

The NIH planning process for the present planning cycle began in September 1979, and will essentially be completed with the publication of this document, the NIH Research Plan, FY 1982-84. The major elements in the process are as follows:

- The core of the process consists of a systematic set of meetings which provide a forum for interaction and decision-making between the NIH Director and the NIH Institute Directors, each with their respective senior staffs. This interaction focuses on each Institute's program plans, opportunities for research progress, proposed allocation of resources, legislative proposals and major program issues. Inevitably, the meetings also enhance the integration of the planning, financial and legislative functions. For each Institute the outcome of this process is a refined program plan, and a planning budget level. The planning meetings initiate action leading to the resolution of or further work on program issues, and they represent a mutually useful briefing in preparation for Congressional hearings.

- A number of health problems cut across the categorical lines of the Institutes and require a somewhat different planning effort. Therefore, another set of activities focuses on the identification of, planning for, and review of these trans-NIH health problems. These health problems are reviewed within the same structure as that provided for the individual Institutes, and each Institute with a program interest in the particular health problem participates. The review centers on the current status of planning in these areas, including the assessment of coordinating mechanisms in place, and the discussion of future activities.

- Budget planning and research planning are integrated at all points throughout the eight-month planning period. This integration provides the NIH with a firmer planning base, a more realistic context in which to consider future program directions, and a more relevant structure around which decisions concerning research opportunities can be made. It also advances the NIH capability to develop the agency preliminary budget submission as a logical follow-through of the planning process.

For the first time, this year, formal planning activities were broadened to include the participation of Institutes' Advisory Council members and of members of the Director's Advisory Committee, who attended the Director's Review Sessions. The contributions which these individuals made added substantially to our consideration of a number of issues. Their participation provided an opportunity for us to hear first hand of many of the stresses that research institutions and universities are now operating under and the possible impact on the community of any changes that the NIH may plan as resources become more constrained. We plan to continue their participation in next year's planning.

DHHS Health Research Planning Initiative

In April 1978, at the annual meeting of the American Federation for Clinical Research, the Secretary of DHHS announced plans for the government, the health research community and the public to embark on the development of a multi-year strategy for health research. The Secretary asked the NIH to take the lead in developing and guiding this initiative. Since then, a number of major planning activities have been undertaken.

- Phase I--Development of Health Research Principles

Draft HEW Health Research Principles were developed in the summer of 1978. These were intended to guide the subsequent activities involved in creating a multi-year strategy and plan for health research. DHEW agencies and staff offices, professional societies, health organizations, other federal departments and agencies and interested individuals all contributed to the draft principles. A National Conference was then held at the NIH in October 1978 to review and comment on the first draft of the principles. The Conference was organized around five major substantive areas, and panels were established to address each area and to receive public testimony. Each panel developed a report and conference staff revised the draft principles based upon the reports and public testimony and published a Conference Report. The Institute of Medicine, National Academy of Sciences, at the request of the Secretary, established a special committee to review and critique the revised principles. Their report was transmitted to the Secretary in early-March and was used in revising the principles. The approval of the final set of principles by the then-Secretary in August 1979 marked the completion of this phase of the initiative.

- Phase II--Health Research Activities of the DHEW--Current Efforts and Proposed Initiatives

This document began with a description of all the health research activities of the Department. It also summarized the organization, mission, and deployment of research resources as provided by each of the nine components of HEW that underwrite or carry out the search for new knowledge relevant to health. The second part contained, for the Secretary's consideration, some research proposals she may wish to identify for special attention in fiscal years 1981-1984. Each proposal was discussed by the Steering Committee and selected from a much larger set for presentation. These proposed initiatives demonstrated how the health research principles could be used in formulating a research plan for the Department. They were not, however, integrated into the specific priorities of each of the Agencies. Eight of the eleven initiatives described in this document are in an advanced stage of implementation or planning. Indeed, some have been in operation for several years. The sponsoring agency, and those agencies listed as cooperating in each initiative, endorsed it and will continue their participation in it. The remaining three proposals were in a more preliminary form. They addressed major cooperative issues, but details of research scope and the nature and extent of other agency participation were not completely determined. This document was published in December 1979, and widely circulated for comment. In addition, a special committee was established by the Institute of Medicine, National Academy of Sciences, to review and critique this document. Their report was submitted to the Secretary, DHHS, in May 1980.

- Phase II Update--Health Research Activities--Current Plans and Initiatives

  This phase of the effort updated the health research initiatives initially proposed. Recent budget developments, comments received, and the Institute opf Medicine critique provided the basis for modifying the proposed research initiatives. In addition, the health research planning processes currently used by each agency represented in this effort are described in this document. Proposals for future directions in Departmental health research planning are also considered. This effort was recently completed and the final document submitted to the Secretary, DHHS, in mid-July.

- National Science Foundation's Annual Science and Technology Report and Five-Year Outlook

  The National Science Foundation is mandated by the Congress to develop an annual Five-Year Outlook for Science and Technology as well as an Annual Science and Technology Report. The first deals with problems, opportunities, and constraints, and focuses on areas of research in which advances over the next five years can be expected to contribute to resolution of national problems; the second covers FY 1980 accomplishments, program plans for FY 1981, and budgetary projections for FY 1982.

  At the suggestion of the National Science Foundation and the Office of the Assistant Secretary for Health, NIH has been designated the lead Federal agency to coordinate preparation of the health research sections of these two reports. Coordination within the Department for this effort will be undertaken by the HHS Steering Committee for the Development of the Health Research Strategy. For the overall Federal perspective on health research, the document will be reviewed by the Committee on Health and Medicine of the Federal Coordinating Council for Science, Engineering, and Technology of the Office of Science and Technology Policy. This committee is chaired by the Director, NIH, and comprises all Federal agencies with health research programs.

  These reports fit logically into the health research planning within the Department; at the same time, this effort responds to the Institute of Medicine's recommendations that there be coordination and collaboration of health research planning among all Federal agencies.

D S Fredrickson

Donald S. Fredrickson, M.D.
Director
National Institutes of Health

Part One

NIH PLANS AND OPPORTUNITIES FOR RESEARCH PROGRESS

INTRODUCTION

This section summarizes the plans and opportunities for research progress in the biomedical research and supporting programs conducted and supported by the NIH Institutes and Divisions. The NIH Research Strategy Plan, 1982-1984, presents an overview of NIH plans for the time period. The general emphasis and direction of NIH activities is discussed, and the major initiatives proposed are presented in terms of the SATT approach. The Strategy Plan was forwarded to the Assistant Secretary for Health in April 1980, and will be incorporated into an overall PHS Three-Year Strategy Plan.

The research strategy paper is followed by discussions of each Institute and Division's program plans and research opportunities. These present highlights of the more comprehensive plans which are developed by the Institutes. Each Institute conducts its own planning process through which future program directions are identified and resource allocations are considered. The Institute planning activities result in a diverse array of program documents which provide more extensive information than the presentations in this section. These separate planning processes feed into the NIH Research Plan cycle and provide the substantive basis for the Director's Review, an annual program review in which the Director, NIH, and his staff meets with the Director of each Institute and his or her staff for intensive discussions on the status of current programs and future plans. The results of these reviews form the basis of the Institute plans presented here. These plans may be modified in the coming year in order to take advantage of new opportunities as they arise and also to reflect Congressional changes in the budget.

The sections contained in the Institutes' plans are:

- Director's Preface--This statement provides an indication of the dimensions of the health problems being addressed by each Institute, highlights the research program strategy developed to deal with the problems, and briefly discusses the relevance of this strategy to broader health objectives.

- FY 1981 Program Changes--This portion of the Institutes' plans highlights major activities that are planned to be initiated, maintained, cut back, eliminated or not started in FY 1981 as a result of the FY 1981 budget process. The intent here is not to address each research program, but to focus on only major program changes. There is also a brief discussion of directives resulting from FY 1980 Appropriation Committee Reports and their impact on FY 1981 plans.

- FY 1982 Program Changes--This portion highlights major program changes planned for FY 1982, including new initiatives, expansion of ongoing activities, shifts in program emphases and cut-backs in program.

- Stabilization--Some Institutes have elected to describe how they will stabilize research project grants in 1981 and 1982, and the impact that this initiative may have on their full range of activities.

- Summary of Director's Review Session--This portion of the plan summarizes some of the plans and issues discussed at the NIH Director's Review Session with each Institute and Division.

Chapter 1

NIH RESEARCH STRATEGY, FY 1982-1984

The health research supported and conducted by the HEW represents a vast and complex enterprise which provides the foundation for improved medical care, better health promotion, and newer disease prevention measures. Support for health-related research and development in the United States, from all sources, reached an estimated level of $6.9 billion in 1979. The Federal Government--the senior partner in the health research enterprise--contributed a little over 60 percent of this national total, industry provided almost 30 percent, and State governments and private nonprofit organizations contributed the remaining 10 percent. The health agencies of HEW contributed approximately four-fifths of the $4.3 billion provided by the Federal Government to the support of health research and development activities in 1979. The Public Health Service (PHS), in turn, accounted for 98 percent of the HEW total.

The National Institutes of Health--the principal medical research arm of the Federal Government--provided almost 88 percent of the PHS total investment in health research activities in 1979. Nearly 90 percent of the annual NIH budget goes to support research and research training at universities, medical centers, hospitals, and other research institutions. About 1,200 institutions in every state in the Nation and in several foreign countries receive NIH funds. The remaining 10 percent of the NIH budget is devoted to the direct support of laboratory and clinical investigations conducted by the staff of the NIH intramural program--one of the largest and most distinguished biomedical research centers in the world.

For the past several years the NIH has been developing and refining a method for classifying and describing the allocation of its resources. As a result of this effort, the activities of the NIH to improve the Nation's health are now classified into four major categories, which, together, comprise the SATT model. The first category, Science Base, accounts for almost 77 percent of the NIH budget. It includes those activities designed to reduce disease and disability through the development of new approaches to prevention and treatment. These new approaches result from the elucidation of mechanisms underlying fundamental biological processes and an understanding of what happens when these processes fail or are altered to produce disease. The primary mechanism for developing this fundamental knowledge is the investigator-initiated research project grant.

The second category, Clinical Application, refers to research activities in which the emphasis is on intervention, including prototype development and refinement of products, techniques, and practices. Examples include development and testing of vaccines; the conduct and support of clinical trials of drugs or other treatment approaches; and improvement of techniques for determining health status. Approximately 12% of the NIH budget is devoted to these activities.

The third category, Technology Transfer, involves the transfer of research findings to the health care delivery system. Transfer activities are thus concerned primarily with the development of technical consensus on new interventions and the demonstration of these new technologies in health care settings. The Office of Medical Applications of Research serves as the focal point for NIH transfer activities and as a link to the broader activities of the National Center for Health Care Technology. Technology Transfer consumes about 5% of the NIH budget.

Training, the fourth major category of NIH activities, accounts for only 5% of the total budget but remains one of the most crucial activities supported by the NIH. The training of biomedical investigators is necessary to guarantee a continuing influx of fresh research talent and ideas.

As part of the NIH planning process, the Director, NIH, conducts an intensive annual program review with each Bureau, Institute, and Division. For the past several years the programs of the Institutes have been reviewed within the framework of the SATT model. Discussion in these reviews focuses on the establishment of priorities along this health research continuum and on the tradeoffs required to implement programs within areas of established priority.

Last year the NIH participated--together with each of the other HEW health research agencies--in a formal planning effort which examined all of the Department's health research activities in order to seek greater cohesiveness and effectiveness in the conduct of these programs. That process culminated in the development of: (1) a set of health research principles intended to provide a conceptual framework for the development of an HEW multiyear strategy for health research; (2) a comprehensive analysis of the health research activities of the HEW agencies; and (3) a set of proposals for special health research initiatives that require the cooperative efforts of two or more of the health agencies. NIH participation in those deliberations and the agreements generated as a result of that process have helped the NIH in planning the future course of its program. It is against this backdrop that the budget was developed for the period of FY 1982-1984.

Program Changes

General

The budget strategy for the period FY 1982-1984, reflects the intent of the NIH to implement the Administration's commitment to sustain activities designed to stabilize the science base. A major part of the science base consists of research supported through investigator-initiated research project grants. These awards have been selected for special emphasis to underscore the Nation's determination to maintain fundamental research as an indispensable long-term societal investment. Demonstration of support for this principle is necessary to assure that young Americans will continue to make the commitment necessary to devote their careers to the health sciences. The ability of the NIH to fund annually about 5,000 competitive research project grants will contribute substantially to providing assurance that the Nation's science base will not be eroded.

The NIH recognizes, however, that research project grants represent only one element--albeit a crucial one--in the multifaceted approach that is required to provide a balanced program of support for biomedical research. Although the science base forms the foundation from which new knowledge is generated, that knowledge must be translated into practical applications, clinical trials must be conducted, technology must be moved into community settings and evaluated, new scientists must be trained, research resources must be maintained, and centers of excellence must be preserved. Each of these imperatives has been considered in the projected resource allocations for FY 1982-1984. In addition, special needs have been identified which will require action by the NIH during the period of this plan.

In recognition of the increasing need to replenish and upgrade the sophisticated equipment required by institutions engaged in biomedical research, the budget provides a modest level of funds to begin improving the instrumentation in extramural laboratories. The NIH, in cooperation with scientists and administrators from research institutions will explore the broader range of problems that beset the research environment. The results of that review will undoubtedly shape the nature of additional actions required during the period of this plan to help stabilize the research environment.

The NIH intramural program must also be buttressed against the ravages of inflation, and its laboratories and clinics must be upgraded to compensate for physical deterioration as well as obsolescence. The intramural program is a valuable instrument in accomplishing the NIH mission and serves as a benchmark of excellence for our Nation's biomedical research community. The scientists, their supporting staffs, and the laboratory and clinical facilities together form an irreplaceable national resource. This plan reflects the need to maintain the intramural program at its current level of effort; to complete the Ambulatory Care Research Facility and continue the modernization of the NIH Clinical Center; and to initiate a program to modernize the NIH laboratory buildings, many of which have been in use since 1940.

Last year, for the first time in six years, stipend levels were increased for training under the National Research Service Award program. An additional increase in stipend levels will be necessary to compensate partially for the effects of inflation.

Specific

Some specific program changes in FY 1982 are provided below. Greater detail will be provided in the NIH Research Plan which is now being developed. The following have been selected to serve as examples:

Science Base

- A specific enzyme defect resulting in high levels of the amino acid ornithine has been discovered in the serum of patients with a form of inherited retinal degeneration which leads to night blindness, a gradual loss of peripheral vision, and ultimately blindness. A dietary treatment directed at the correction of this defect has been developed and will be tested.

- Research on the cause and prevention of cancer will emphasize studies to understand the control of certain genes capable of causing cancer. Such genes will be isolated and identified using recombinant DNA technology.

- A research effort will be initiated to elucidate the roles of neuroendocrines on the control of brain function and on the control of organ function by the brain.

- Molecular and clinical aspects of gerontological and geriatric dermatology will be studied to understand basic mechanisms of dermatologic aging and to facilitate the prevention, diagnosis and management of age related skin disorders.

- Specialized Centers of Research will be expanded in fibrotic and immunologic diseases, cystic fibrosis, chronic obstructive lung diseases, and pediatric pulmonary diseases.

- Opportunities will be exploited to use new technologies to achieve mastery of the immune system, for application to infectious disease problems. These technologies include recombinant DNA and hybridoma cell fusion.

- Priority will be given to improving the availability to biomedical scientists of the latest technologies through nationally shared Biotechnology Resources; making Biomedical Research Support Grant funds available in the most effective manner; stabilizing the availability of resources for clinical research; and, meeting the national research need for primates.

- Research studies will be undertaken to determine the potential role of commonly prescribed drugs, such as antibiotics, and environmental agents, such as heavy metals, in producing kidney toxicity and subsequent kidney disease.

- A research grant program has been initiated in biomedical communications. Support will be provided for basic studies of the utilization of computers in medicine to solve problems in automated information retrieval, indexing, and related subjects.

- A program of research will be initiated on psychological, psychobiological, and social development of women from infancy to maturity. A significant component of this initiative will be devoted to women's roles and fertility in order to improve understanding of both determinants and consequences of fertility behavior on an individual and couple basis.

Clinical Applications

- A clinical trial is being designed to evaluate and compare different styles of intraocular lenses and the alternative surgical techniques used to implant them, with particular emphasis on long-term safety and complication rates.

- Clinical trials of promising anti-epileptic drugs will follow drug synthesis and testing programs presently underway.

- Epidemiologic studies are planned to examine the use of prescription drugs and factors related to their use in persons over 65 years of age.

- Donor-recipient compatibility in platelet transfusion therapy will be studied to determine which patterns of platelet transfusions are most clinically beneficial and most cost-effective, to assure optimal transfusion therapy for patients requiring long-term platelet support.

- A large scale cooperative study on interferon and other antiviral therapies of genital herpes infections will be undertaken.

- A multi-center, collaborative clinical trial will be initiated to evaluate the efficacy of total parenteral nutrition, defined formula diets, and other modes of nutritional support in patients with inflammatory bowel disease or short-bowel syndrome.

- A cardiovascular disease (CVD) nutrition research unit will be established for the study of nutrition and heart and vascular disease to achieve close interaction and collaboration between investigators in CVD and nutrition, and to offer a broad range of research training activities oriented toward human nutrition in health and disease.

- The Biological Response Modifiers Program will increase the number of biological materials evaluated experimentally and clinically. Such agents will include (a) agents which augment immunity, modulate components of the immune response and induce or restore affectors of immunity; (b) interferons and cytokine products; (c) thymic hormones or factors; (d) tumor-specific vaccines and immune effectors in the form of tumor or stem cells; (e) agents which interfere with carcinogenesis; and (f) agents which modify tumor clonogenicity and/or the maturation of tumor or stem cells.

Technology Transfer

- The National Library of Medicine serves as a critical national resource for the dissemination of biomedical information to scientists and practitioners active in research, education, and health care delivery environments. Emphasis will be placed on expanding and improving library and information services through the acquisition, preservation, organization, and dissemination of biomedical literature.

- Five current clinical trials on the treatment of several serious ocular disorders are expected to generate results which will be ready for broad dissemination to practitioners and patients. These are: the Diabetic Retinopathy Vitrectomy Study, the Macular Photocoagulation Study, the Branch Vein Occlusion Study, the Evaluation of Timolol in the Treatment of Glaucoma, and the study of the Role of Vitamin E in the Treatment of Retrolental Fibroplasia.

- A number of consensus development conferences will be held, among them:

  -- one on computerized tomography of the central nervous system. The state-of-the-art will be examined and information will be developed on the use of the technique for professionals and the lay public.

  -- one on how to minimize the medical and socio-economic impact of infections of the urinary tract during pregnancy.

  -- and one for orthopedic surgeons, to clarify optimal technologies for replacing irreparably damaged arthritic joints with implanted artificial joints.

- On the basis of data obtained from the Epidemiologic Study of Sudden Infant Death Syndrome (SIDS) Risk Factors, and on hypotheses formulated by the Study's steering committee and consultants, presentations of findings are planned for the research and clinical communities.

- Smoking cessation programs will be developed, designed specifically for populations of smokers who are at special risk for cardiovascular disease because they not only smoke, but also present other exacerbating risk factors.

- A field evaluation, including cost-benefit analyses, will be conducted on new techniques for using fluoride in the prevention of dental caries.

Training

- Emphasis will be placed on programs designed to increase research manpower in immunology, epidemiology, toxicology, biostatistics, psychophysics, and possible shortage areas in the visual sciences.

- The retention of physicians in laboratory and clinical research should be partially facilitated as a result of implementation of the Clinical Investigator Award which provides support to help new clinical investigators make the transition from training status to that of established investigator.

- Support will be expanded for recently established career award mechanisms in diabetes, such as the Special Emphasis Research Career Award (SERCA) and the New Investigator Research Award (NIRA). A comprehensive manpower development program will be established to provide a continuum of research training in diabetes and related diseases, starting with periods of short-term training to attract undergraduate science majors; continuing through graduate education and post-graduate traineeship-fellowship awards; and progressing into "starter" grants for independent research.

- At the same time, the NIA and the NIAMDD will initiate a special emphasis research career award program aimed at encouraging qualified individuals to develop research interests in problems specifically related to diabetes and aging.

Program Linkage

Last year marked the culmination of the second phase of an extensive effort to develop an HEW Health Research Strategy. The development of this strategy was guided by an HEW Steering Committee chaired by the Director, NIH, and consisting of all PHS agency heads, the Assistant Secretary for Management and Budget, the Assistant Secretary for Planning and Evaluation, and the Administrator of the Health Care Financing Administration.

The first phase of this effort, initiated in April, 1978, resulted in the development of a set of principles to guide health research investments by the Department. The second phase produced a research planning document which presented for the first time a description of all HEW health research activities within a single framework and contained a set of proposed "health research initiatives" which represent important experiments in cooperative research planning and management. Subsequently, the NIH participated in the planning, implementation, or expansion of several of the special health research initiatives suggested by the HEW planning effort. Included among these are:

- Stabilization of the Science Base--A key initiative in the HEW health research planning document related to stabilization of support for research grants. The purpose of this initiative is to introduce a greater degree of stability and predictability into the funding of science base activities by the NIH, ADAMHA, and the HRA. With a strong endorsement from the Administration and the Congress, the NIH has begun to implement the stabilization initiative. The FY 1981 budget request for the NIH places a major emphasis on providing funds to support approximately 5,000 competitive research project grants or about one-third of all approved grant applications. This emphasis will be continued in subsequent budget requests.

- National Toxicology Program (NTP)--The goal of the NTP is to strengthen HEW activities in the testing of chemicals of public health concern. Under the leadership of the Director, NIEHS, the program comprises the relevant activities of the FDA, CDC/NIOSH, NCI, and the NIEHS. An increase in funds requested for this program in FY 1981 will permit an acceleration of the rate at which bioassays for carcinogenicity are conducted. The National Library of Medicine's Toxicology Information Program is providing specialized information support to the NTP.

- Low-Level Ionizing Radiation--The Committee on Federal Research Into the Biological Effects of Ionizing Radiation, chaired by the Director, NIH, was assigned responsibility for conducting an evaluation of all current Federal efforts in ionizing radiation research. Subsequently, a planning team, chaired by the Director of the National Cancer Institute, was established to develop the major objectives of an expanded and intensified research program on the biological effects of low-level ionizing radiation and to coordinate HEW activities in this area of research.

Additional examples of NIH participation in special cooperative health research efforts include:

- Role of Nutrition in the Development of Gallstones--The NIAMDD has developed plans for an epidemiological study of the relationship of diet to the development of gallstones. It is anticipated that the study, carried out in cooperation with the National Center for Health Statistics (NCHS), will utilize the results of the NCHS's Health and Nutrition Examination Survey (HANES) to yield information helpful in preventing this disease through diet modification and other means.

- The Interagency Committee on Population Research (ICPR)--This committee, chaired by the Director of the Center for Population Research, NICHD, serves effectively to facilitate exchange of information in population research, coordinate research activities, analyze Federal population research activities, and make recommendations on research efforts required in the population sciences.

- The Interagency Diabetes Mellitus Coordinating Committee--
  Chaired by the Associate Director for Diabetes, NIAMDD, the Committee prepares an Annual Report which contains a complete compendium of diabetes-related research projects and activities comprising the total Federal effort in diabetes. These Reports permit identification of areas being supported by more than one agency. Such data are helpful in promoting cooperation, coordination, and efficiency in the National Diabetes Program. Examples of such cooperative efforts include:

  -- Several Diabetes Research and Training Centers supported by the NIAMDD are developing collaborative programs with the Diabetes Control Program of the Center for Disease Control (CDC).

  -- The NIH, the National Center for Health Statistics, and non-profit health groups are collaborating, through the auspices of the National Diabetes Data Group, on the analysis of data and the design of future surveys to achieve a more accurate description of the health impact of diabetes.

  -- The National Eye Institute (NEI), through a cooperative arrangement with the CDC, has transferred funds to the CDC to establish a central laboratory to perform tests in support of the NEI's Early Treatment Diabetic Retinopathy Study.

- The Interagency Technical Committee (IATC) on Heart, Blood Vessel, Lung, and Blood Diseases and Blood Resources--This Committee, established by Congressional mandate, provides a forum for communication among the diverse Federal components of the total National Program. Working groups of the IATC have been established to focus the combined expertise of various health-related Federal agencies upon specific issues or areas of the Program and foster the development of collaborative approaches to meeting specific program objectives.

Budget

DHHS - National Institutes of Health

1981 Continuing Resolution
(Budget Authority in thousands)

National Cancer Institute	$1,001,330
National Heart, Lung, and Blood Institute	560,264
National Institute of Dental Research	71,206
National Institute of Arthritis, Metabolism and Digestive Diseases	371,993
National Institute of Neurological and Communicative Disorders and Stroke	253,838
National Institute of Allergy and Infectious Diseases	232,355
National Institute of General Medical Sciences	335,676
National Institute of Child Health and Human Development	223,565
National Eye Institute	120,254
National Institute of Environmental Health Sciences	97,269
National Institute on Aging	76,091
Division of Research Resources	184,439
John E. Fogarty International Center	9,138
Subtotal	$3,537,418
National Library of Medicine	44,730
Office of the Director	22,549
Buildings and Facilities	11,750
TOTAL, NIH	$3,616,447

Chapter 2

NATIONAL INSTITUTE ON AGING

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Chapter 2

NATIONAL INSTITUTE ON AGING

Director's Preface

Five years have elapsed since the National Institute on Aging (NIA) was established with the authority to conduct and support biomedical, social, and behavioral research and training related to the aging process and the diseases and other special problems and needs of the aged. During this time, the NIA has become the focal point within the Federal Government for research on aging. In response to its mandate, the NIA has established programs in biomedical research and clinical medicine, social and behavioral research, and epidemiological, demographic, and biometric research. The biomedical and clinical program focuses on research related to the basic aging processes, physiologic changes with age, including immune, neural, and endocrine functions, and clinical problems, such as nutrition, and drug interactions and utilization, and the special medical problems of the aged. The program on social and behavioral aging supports research on the psychological and social aspects of aging as a process; the behavior, attitudes, and status of older people within a changing society; and the relationships between aging individuals and social institutions. The epidemiology, demography, nd biometry program coordinates and conducts quantitative population based research on health and disease in the aged. In addition to clinical applications of population research, this program conducts demographic and economic analyses.

Significance of the Health Problem

During this century the average life expectancy has increased remarkably. Whereas a child born in 1900 could expect to live 47 years, in 1970, just seven decades later, a newborn could expect to live more than 70 years. However, the subsequent dramatic increase in the number of older persons presents a set of challenges to the health sciences and to the larger society. Individually and as a group, older people must cope with varied stresses--physical, psychological, social, and economic--which threaten their health and sense of well-being. The accumulation of stressful factors with age results in unique needs and problems, including an increased incidence of almost all chronic diseases and numerous difficulties of physical and social functioning. Although those 65 and older comprise 11 percent of the population, their personal health care costs are disproportionately high, amounting to approximately 30 percent of the nation's total. In 1977, expenditures for older people amounted to $41.3 billion, with $27.6 billion coming from public funds.

Research Program Strategy

Althouth the research responsibilities of the NIA are broad and complex, its funds are limited relative to this responsibility. Therefore, the Institute's research program strategy seeks to maximize cooperation and collaboration with other Institutes, agencies, and organizations in addition to working alone toward research objectives. NIA has developed cooperative working

relationships in the areas of disease diagnosis and treatment, training in geriatrics for health professionals, and data bases and populations for epidemiologic and demographic research. The Institute is also involved in a Departmental planning effort for the 1981 White House Conference on Aging. A second important component of the NIA research program strategy, directed by the Research on Aging Act, is information dissemination to researchers, the elderly, the media, and the general public. NIA's public information program includes the transfer of knowledge related to consensus development activities, research opportunities and results, and the practical health concerns of the elderly.

Among the Institute's highest priorities over the next two years will be the development of an updated program strategy for the NIA. This will involve a comprehensive review of the NIA extramural and intramural research programs and will result in recommendations regarding the NIA's future development.

Research Goals

Two primary and related goals of the NIA research program are the enhancement of the quality of life for older people and the containment of health care costs. Greater understanding of the mechanisms underlying time-dependent and age-related changes will result in a delay of the onset of a variety of disease states and reduce their duration and severity. Approximately one million aged are now in nursing homes, comprising 89 percent of the nursing home population, and exceeding the number of patients in the nation's acute care hospitals at any given time. The cost of this care was $13 billion in 1977, with $7.2 billion of this amount coming from public funds. Ultimately, research on aging will reduce the degree and duration of physical, social, and economic dependency, and enable individuals to live free, independent, and healthy lives for as long as possible. In this sense, research on aging is not simply a cost containment measure, but represents the ultimate service to older people, their families, and society.

FY 1981 Program Changes

Major Activities to be Initiated, Maintained or Expanded in FY 1981

- Neuroscience--This program will intensify its development of research in the areas of senile dementia, sleep, and hearing in cooperation with the several Institutes and agencies that are directly involved in these areas or capable of providing the basis for technologic advancement or transfer.

  -- Senile Dementia: Utilizing the current base of intramural and extramural research in neuroscience and senile dementia, the NIA, in cooperation with NINCDS and NIMH, will increase its support of biomedical, behavioral, and social research in Alzheimer's disease and

the dementias of aging. Studies in neurochemistry, cerebral circulation and metabolism, neuroendocrinology, immunology, virolosy, and genetics will be extended and intensified to further define the etiology and pathogenesis of these disorders. These studies will involve cellular and animal models as well as clinical investigations. Behavioral and social research will be expanded as will epidemiologic studies and efforts to improve diagnosis, treatment, and management.

-- Sleep: A broader base of research will be developed to study specific functions of sleep in the elderly and the mechanisms of sleep pathologies associated with aging. The program will emphasize survey studies of sleep disturbances, and the development of better instrumentation and animal models to study sleep.

-- Hearing: In collaboration with NINCDS, the NIA plans to develop a research program to study presbycusis. These studies will initially focus on the acquisition of more precise incidence and prevalence data on hearing loss with age. This effort will be complemented by studies to investigate age-related changes in anatomic structure, physiological function, and psychological response. Improved diagnostic techniques and hearing devices and aids should result from these studies, as well as enhanced instrumentation capabilities through interactions with NASA.

- Genetic Mechanisms--NIA's support of studies on genetic mechanisms involved in longevity and senescence will be substantially increased. The biological models now under development to explore underlying genetic mechanisms will provide the basis for expanded studies using plant, cellular, and invertebrate models, as well as more complex mammalian systems (e.g., chimeric and mosaic animals, expecially mice). In addition to defining genetic mechanisms responsible for longevity and senescence, these studies will explore the influence of environmental factors on genetic expressions of aging.

- Geriatric Medicine and Dentistry--The program in clinical investigation and academic geriatric medicine and dentistry will be further developed to support a broader base of study on the medical and dental problems of the elderly. In cooperation with NIDR, a geriatric dentistry research program will be established to support and complement the developing research program on the clinical and medical problems of the aged.

- Animal, Cellular and Biological Materials Resources--The development, characterization, monitoring and availability of animal, cellular, and biological materials will continue to emphasize the special and continuing needs for these resources to support an increasingly sophisticated research program in biomedical and behavioral aging. Primary guidance for the selection and development of mammalian species to study aging will rely heavily on the National Academy of Sciences Institute for Laboratory Animal Resources report on relevant and appropriate animal models for research on aging.

The program on animal resources will emphasize mammalian species and invertebrate models. This will include the development of better defined rodent species, non-human primate resources, and cats for studies on nutrition, endocrinology, immunology, senile dementia, hearing, sleep, and social and behavioral aging. Invertebrate resources, such as the nematode (C. elegans) and Drosophila, are necessary for the development of studies on the genetic basis of aging and, therefore, will be expanded.

The cellular resources program will give increased attention to the development, availability, and quality control of fibroblasts-like undifferentiated cell resources and cell line repositories, as well as the exploratory inquiry into the culture of differentiated cells.

Both cellular resources and biological materials will be made available, specifically ly-antisera, for support of immunology investigations. Other materials will be provided such as banked tissues, organs, and fluids from various animal resources supported by the NIA.

- Endocrinology--Research on endocrinology will shift to give emphasis to a broader program of research on endocrine function, brain peptides, hormone dynamics, the effects of endocrine imbalance on pathophysiologic processes, and functional responses of target tissues. A recent consensus conference on estrogen use and the menopause focused on some of these issues in an evaluation of menopause; alternatives to estrogens, optimal regimens of estrogen administration, and the conditions for their use.

- Social and Behavioral Research--The social and behavioral research program will undergo major changes in direction and emphasis during FY 1981. Initiated during FY 1980, the new program will stress increasingly sophisticated research on those social, cultural, and psychological factors that affect the process of aging and the health and well-being of older people. The program has three major areas: older people in the changing society; the social and psychological components of the aging process; and the roles of older people in major social institutions such as the family and the workplace. Studies in these three areas will draw upon the established and empirically based disciplines of sociology, psychology, anthropolicy, history, economics, political science, geography, epidemiology, and demography.

  Within these areas, the program will emphasize: (1) the dynamic nature of aging, and differences in the aging process among cohorts born at different times; (2) the interrelatedness of old age with earlier ages, and the interdependence of older people with people of all ages; (3) the variability of aging within our own society and across societies, and the nature, conditions, and flexibilities of sociocultural constraints upon the aging process; and (4) the multiple facets of aging, as social and psychological aging processes are in continuing interplay with biological and physiological aging.

The program will strengthen cooperation with related programs on biomedical research and clinical medicine; on epidemiology, demography, and biometry; on intramural research; and on such overarching NIA interests as nutrition, differential life expectancy, geriatric medicine, and health promotion and disease prevention. Previously initiated emphases that will be continued include work and retirement, minority aging, and bereavement and aging.

- Epidemiology, Demography and Biometry--The primary focus of this program, quantitative population based research on health and disease in aging, will be further developed in FY 1981. A cooperative study with NHLBI on systolic hypertension in the elderly is planned to evaluate whether therapy to lower blood pressure reduces specific nonfatal morbid events or influences mortality in the older population. NIA will continue to cooperate with other Institutes on the follow-up study of the older population in the Health and Nutrition Examination Survey (HANES) to acquire and evaluate information on morbidity and mortality outcomes associated with nutritional status. Related ongoing studies in several reference populations, in which selected demographic, health, and psychosocial characteristics have been established, will provide comparative cross-sectional data for evaluation of the HANES study and provide the baseline for integrated studies of medical, socioeconomic, and behavioral aspects of health. The study on senile dementia, which is acquiring and analyzing data on the prevalence of senile dementia in an adult community, will be maintained at the current level, as will the epidemiological study analyzing the events surrounding the last days of life.

  Population dynamics and research analysis dealing with demographic economic factors will be maintained at the FY 1980 level of activity. These studies, utilizing for the most part existing data sources, will continue the analysis of data banks and sources in order to exploit their utilization in assessing demographic and economic changes and social and medical factors that increasingly impinge on aging cohorts. Efforts to develop research data bases and extract and analyse Federal and non-Federal data, study cohort survival and factors related to survival, and analyze the economic ramifications of the demographic shift toward an aged population will be maintained.

- Research Training--NIA training programs will undergo a change in direction and emphasis as a result of previous advice and guidance from training program directors, Advisory Council members, and expert consultants. The research training effort will be aimed at administrative and substantive means to improve research training, integrate predoctoral and postdoctoral training with program objectives, and develop means of attracting M.D.s to research training in clinical investigations such as geriatrics, nutrition, endocrinology, and pharmacology.

Major Activities to be Cut Back in FY 1981

No new grants will be made for the Geriatric Medicine or Dentistry Academic Awards, Clinical Investigator Awards, or training grant awards (individual or institutional fellowships) during FY 1981 in order to preserve the funding level of research project grants.

Impact of FY 1980 Appropriations Committee Reports

The major implications of the Appropriations Committee Reports for the FY 1981 budget is the increased support of investigator-initiated research projects and resource development. The House Appropriations Committee indicated that research funding attention should be given to support of aging and disease (cancer, diabetes and senile dementia), epidemiology of aging and disease, animal resource development, and clinical nutrition.

FY 1982 Program Changes

The following activities are planned for FY 1982:

- Nutrition--One of NIA's main activities will be the expansion of the research program on the relationship between nutrition and the health of the aged. Support of the follow-up HANES study should make it possible to support more definitive survey studies on the special dietary needs of the elderly, and permit exploratory research on the relationship of specific dietary deficits to health. Collaborative studies between nutritionists, social scientists and neuroscientists will provide the basis for studies on the influence or effects of neurologic factors, environment, and sensory deficits on dietary habits.

- Exercise Physiology and Musculoskeletal Function--Studies of exercise and functional changes in the musculoskeletal system often neglect integrative research into the relationship of psychological, physiological, and social factors and exercise and aging. Therefore, the NIA will begin to develop studies in cooperation with other Institutes and agencies to interrelate nutrition, endocrine function, cardiovascular efficiency, and functional changes in the central nervous system, and social and psychological variables with exercise and aging.

- Social and Behavioral Research--Building on the 1981 expansion, the social and behavioral research program will develop grant initiatives through workshops, position papers, and program announcements in such highly promising research areas as cross-cultural variability of aging processes; the aging brain in relation to social and behavioral aging; life-course patterns of education, work, and retirement; social support systems as they affect health; social components of geriatric medicine; and critical methodological obstacles in aging research. Updated inventories of the accumulating social science knowledge will be published, pointing to gaps needing further research and to implications for professional practice and public policy. Training support will be

initiated for research on age in the population (e.g., mortality, morbidity, migration; rural-urban residence; divisions by sex, race, ethnicity, socioeconomic status) and on behavioral medicine and medical sociology. Resources will be developed and utilized primates, as models for studies of social and psychological aging and age-related social structures; and computerized data archives, to facilitate secondary analysis of already available information on aging.

- Epidemiology, Demography and Biometry--In view of the cumulative project-by-project involvement of a limited staff and funds, the level and focus of program activity will essentially remain unchanged from FY 1981. The economic analyses related to health cost containment and the effects of age structure in the U.S. population will be curtailed. Research programs on long-term care alternatives, data archiving, and hypothermia may be established.

Summary of NIA's Research Plan Review Session with the Director, NIH

Program Overview

Some general issues were highlighted that would be important for the Institute over the coming year.

- The National Aging Advisory Council has begun annual reviews of Institute programs, thereby strengthening and expanding their advisory role.

- A reorganization to separate program and review elements in the extramural program area is pending. It should also be mentioned that the Institute feels it has achieved a reasonable payline for research project awards.

- The Department's intention, were the Space Technology for the Elderly Act passed, would be that the AoA rather than NIA be designated as lead agency to determine application of NASA technology to needs of the elderly, such as in the area of prosthesis research. Because of research it supports on prosthesis, NIA maintains a strong interest in the field of biomedical engineering.

- Although the intramural programs of the National Institute on Drug Abuse is planning to locate at the Baltimore City Hospital and a coalition will be occuring between the respective research activities in the future, there currently is not a "critical mass" of biomedical research at the facility. In view of the city government's consideration of other uses for this property, it would be important to have a program there that would involve more than NIA.

Stabilization of the Science Base

A major portion of the discussion focused upon the proposal to stabilize NIH support of the science base, especially as it applies to providing predictable funding for research project grants.

With a constrained budget, the NIA would support a modified approach to the stabilization of the science base because of what it feels is the special status of aging research. NIA is the youngest Institute, and therefore, most of its research is of recent origin and almost exclusively in the science base category. It has considerably less flexibility to exercise some of the options available to more established Institutes with special or long-existing programs, such as centers and collaborative research efforts, in protecting its research project grants.

For example, many research projects supported by the Institute are dependent upon special aged animal and cellular resources funded by NIA research contracts. If contract funding were decreased with a concomitant reduction of these biological resources, such research projects would have to be terminated.

Reestablishment of these resources, such as aged animal colonies, would require a minimum lead time of 2 1/2 to 3 years. Other NIA contracts fund epidemiology and biometry research. This support can be reduced only so far, beyond which point this entire research effort would have to be dropped in midstream. Therefore, in the case of NIA, funding of R & D contracts cannot be considered separately from support of research project grants and the science base. Consequently, NIA would propose to sacrifice a portion of research project grants over the short term in order to preserve other important elements of the science base over the long term.

It is of special concern that potential effects of the stabilization proposal on NIA's program activities would place the Institute in too limited a growth pattern in its formative stages. Therefore, this proposal will continue to be examined to determine ways it can be made sensitive to special needs of Institutes.

Manpower Development/Training

Trained manpower was highlighted as one of the Institute's most crucial needs.

- Training--Because gerontology is not a medical specialty and research on aging touches on several biomedical disciplines, there are no clearly identifiable departmental locations for training. The Institute, therefore, strongly supports the use of the institutional award as a training mechanism. Currently, training grants are supporting slightly more individuals in the social sciences than in the biological sciences.

- Manpower development--Senior Fellowship awards will be used to interest experienced scientists from other fields in aging research. Geriatric Medicine awards are proving successful as a mechanism in developing curricula on gerontology and incorporating geriatric medicine into medical school study. NIA views these awards as establishing a resource which will ultimately encourage and enhance research. Eleven schools received Geriatric Medicine awards in FY 1979 and there are plans to make several more awards in FY 1980. A similar program with one award in the area of geriatric dentistry was recently announced by the Institute.

Consensus Activities

- The conference on long-term estrogen use held in the fall was quite successful and useful to NIA in considering future studies. Some research possibilities were identified as a result of the exercise, but these may be deferred because of ethical issues and other complicated scientific questions.

- New consensus efforts that are being considered include criteria for admission into nursing homes--medical versus social criteria, and the use of psychotropic drugs in nursing homes.

- Legislation with regard to the retirement age of airline pilots (The Experienced Pilots Act), would mandate NIA to examine existing data to determine functional measures of age. The Institute proposes that the study be undertaken as a consensus development project.

Major Civil Rights and Affirmative Action Initiatives

An agreement has been reached recently between NIA and NEI to share the services of an EEO coordinator. Presently, the Institute contributes to the MARC and MBS programs and is working on improving women and minority staff ratios.

Dr. Schimke and Mr. Takamura, members of the National Aging Advisory Council, participated in the review session. Their views provided a broader perspective on the issues discussed.

Chapter 3

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

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Chapter 3

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Director's Preface

Disease prevention is one of the top priorities of the Public Health Service and the National Institute of Allergy and Infectious Diseases (NIAID) research programs directly support this effort. The objective of the Institute's research programs is to acquire the knowledge necessary to lift the barriers that block current efforts to treat and prevent infectious, allergic, and other immunologic diseases. This research is also beginning to reveal the complex role of immune processes and infectious agents in a broad spectrum of diseases that affect many organ systems.

One hundred years ago, Pasteur, Erhlich, and Bordet recognized the interdependent nature of infection and immunity. This close association between infectious processes and immune mechanisms remains a central theme which knits together the diverse programs of NIAID. Thus, recombinant DNA technology, a legacy of E. coli genetics research, has unraveled the genetic complexity of immunoglobulin synthesis. And hybridoma cell cultures, an outgrowth of immunology, are used to produce monoclonal antibodies now employed as versatile reagents to examine the antigenic complexity of microbes, including parasites. These powerful techniques will be employed to explore the biochemical determinants of infectious diseases, the chemical basis of immunoregulation and, indeed life processes in health and disease. From this knowledge will emerge new opportunities to diagnose, treat, prevent and control infectious diseases and allergies, as well as other disorders that involve alterations in immunological processes. Pasteur's first century has been crowned with glory. We move into the second century with an historical precedent for optimism.

The public health importance of asthma and other allergies and infectious diseases need not be reviewed again in detail. Infectious diseases continue to be the first cause of morbidity in the United States and the most common cause of morbidity and mortality in the world at large. In 1975, the incidence of infections in the U.S. was estimated at 462/1000/annum. In addition to common acute diseases such as gonorrhea and the common cold, bacterial and fungal infections are serious complicating factors in the management of the underlying chronic diseases such as diabetes, cancer, arthritis and cystic fibrosis. There are at least 100,000 new cases of bacteremia in our hospitals each year due to opportunistic gram negative organisms. Beyond the shores of the United States, a diverse group of infectious diseases takes a dreadful toll in the developing countries and hinders social and economic development.

Recent health statistics emphasize the socioeconomic importance of immunologic disorders. Asthma and allergies account for approximately 5 percent of all physician visits. In 1975, the direct cost of this care including hospitalization was $1.5 billion dollars; by 1982 this figure will have increases substantially. The toll of days of disability due to these diseases at the

very peak of learning capacity and productivity is not generally recognized. In adults, asthma alone accounts for at least 90 million days of restricted activity and absence from the work force.

A major but as yet unmeasured proportion of chronic diseases (e.g., rheumatoid arthritis, systemic lupus erythematosus, and possibly juvenile onset diabetes) are probably due to a complex interplay between infection and immunity. For this reason it is difficult to gauge fully the social and economic impact of infectious and immunologic diseases. Morbidity and mortality, and direct and indirect cost figures are at best rough estimates of the true burden.

Recognizing the viruses are the most frequent cause of infections in the United States, the Institute has developed a new strategy for the treatment and prevention of virus diseases. Utilizing the recommendations of the Virology Task Force, the NIAID Council identified eleven priority research areas, including training. Special attention was focused on vaccine development, antiviral drugs and the use of viruses as research models and tools to examine life processes.

Emphasis on virus infections has not diminished our sensitivity to the new problems in bacterial infections, such as the rising tide of sexually transmitted diseases and the emergence of widespread antibiotic resistance among many pyogenic bacteria. For example, a working group has been actively examining current research on sexually transmitted diseases and will make recommendations to the Council on research initiatives.

The Institute's Task Force on Asthma and Other Allergic Diseases developed a broad research strategy to advance knowledge of the underlying allergic mechanisms and to exploit new opportunities for diagnosis, prevention and treatment. Our Council has developed recommendations for diverse research and training initiatives in fields ranging far beyond the traditional domains of asthma and allergy, such as drug allergy, dermatologic allergies, occupational/environmental asthma and related respiratory diseases (e.g.; farmer's lung).

Specific strategies described thus far have been concerned with only a few of the many important health problems which are the responsibility of the Institute. To attack this array of issues on a broad front, the Institute's overall strategy relies on free-ranging research in microbiology and immunology. After extensive discussion with expert groups and the Advisory Council, special areas are selected where there are opportunities to hasten the application of basic science to clinical medicine. This overall effort requires a continuing replenishment of scientific talent, including physicians trained in the new research technologies, through the training programs supported by the Institute.

FY 1981 Program Changes

The FY 1981 Planning Assumption is about 6.5 percent above the corresponding level of FY 1980. But it is the ecology of science, including some long term changes, rather than this modest increase which is creating the prinicipal planning problems for the Institute.

First, the relentless expansion of research costs is, in part, a reflection of consumer price index changes generally, but also an increase in sophistication of research methods and equipment. Between FY 1977 and 1978 the cost of an average NIH project in immunology and virology rose 26 percent. Additionally, new equipment needs and facility obsolescence will increase the demand for funds.

Second, for ten years, the Institute has seen a steady increase in application pressure as measured by the number of approved applications. In the past 5 years this flood of good ideas, from an enlarging number of investigators, has increased nearly 50 percent.

The increase seems to have two origins: one is the perception that the traditional disciplines supported by the Institute--virology and immunology--are either in a phase of expanding scientific opportunity, or like parasitology, are in the process of a rebirth. The other reflects a change in the source of support for science. NCI has been the leader in support of virus research related to oncogenesis; however between 1977 and 1978 the NCI virology portfolio decreased by some 266 projects. The entire NIAID virology portfolio in 1978 numbered only 283 projects. An unknown number of these cancer virologists can be expected to seek support for less categorical studies.

Third, the convergence of application pressure (stemming from an increase in the number of investigators as well as expanding scientific opportunities), increased cost of doing research, and a level budget will result in a decrease in the proportion of approved applications which can be funded. The resulting disappearance of research career opportunities will become a self feeding, destructive cycle--"there is no future in a research career."

Fourth, certain areas of research, such as allergies, sexually transmitted diseases and tropical medicine, are of major medical and social importance. Yet, they lack any significant public or private source of funding other than the Institute.

Major Activities to be Initiated in FY 1981

Although some funds above the commitment base will become available in FY 1981, these are channeled to new and competing regular research projects and no wholly new programs will be initiated. In recent years a series of task force reports on immunology, virology, allergic and sexually transmitted diseases have mapped ambitious plans. The substantial budget increases of FY 1979 and 1980, while still far below the recommended levels of funding, have greatly enlarged the assault on a wide range of problems. Stabilization of the science base is one of the Secretary's Health Research Planning Principles. With some 36 percent of its approved research grants funded in 1980 the Institute has in effect stabilized support only of the research grants portion of the science base, even though such stabilization will mean a loss of the momentum built up in recent years in the areas of Applications, Transfer and Training of the SATT paradigm.

Major Initiatives to be Maintained in FY 1981

The Institute will maintain its commitment base of support of high quality investigator-initiated grant applications, including research on immunologic and viral aspects of diabetes and other chronic diseases. Commitments for the recently expanded Tropical Disease Program, including Tropical Disease Research Units and International Collaboration in Infectious Diseases Research, will be met as well as those for an Arbovirus Research Unit, Centers for Interdisciplinary Research on Immunologic Disease and the recently recompeted Asthma and Allergic Disease Centers and Sexually Transmitted Disease Research Units.

Major Initiatives Which Must be Cut Back in FY 1981

The decision to stabilize the research grants portion of the science base and provide support for an increasing number of high quality proposals will require a general cutback of special programs which focus attention on complex problems, such as evaluation of antiviral drugs or chemotherapeutic agents, vaccines and transplantation procedures. Among the areas that must be cut back are additional new initiatives developed from Tropical Disease Research Units, Asthma and Allergic Disease Centers, as well as systematic research into prevention of infant infections and immunodermatology (pathogenesis of immunologically mediated skin diseases precipitated by environmental agents).

Contracts are used to develop new products or for support of the multicenter clinical trials which move research discoveries into general application by proof of efficacy, safety and feasibility. FY 1981 funding will require a reduction in the total amount for contracts and will not allow for any new contracts. This will indefinitely delay the plans for such trials as those for amantadine/rimantadine chemotherapy in influenzal pneumonia, interferon for cytomegalovirus infections in renal transplant patients, new antivirals for herpes genitalis, and influenza vaccine in the high risk populations. The funding situation will also prevent further exploration of interferon inducers or development of reagents for allergenic studies and will delay risk assessment of recombinant DNA research.

Possibly the most exciting development since the discovery of recombinant DNA technology is the hybridoma technique. This method leads to the creation of versatile replicating hybrids by fusing a myeloma cell capable of immunoglobulin production with an antigen sensitized lymphocyte even of a different species. This development will have great practical as well as theoretical value. Bulk cultures of such replicating chimeras will become a source of exquisitely specific antibody for use: in immunotherapy of infectious or malignant diseases; in diagnosis and epidemiologic survey; and in laboratory experiments to study pathogenesis and immune processes. Provision of resources for this type of work was initiated at minimal level in FY 1980 but cannot be adequately pursued as planned despite the great interest of investigators flooding into the field.

The long established transplantation program has revealed that while matching for the major histocompatibility locus (MHC) is important, other non-MHC and tissue specific antigens are being recognized and can cause draft rejection. It will not be possible systematically to study and categorize these and provide reagents.

In regard to training, only about 390 trainees can be maintained in the training pipeline under the 1981 budget plan. Such a program will "graduate" about 170 newly trained investigators per year for academic, industrial and federal research institutions, including NIAID. This is about 36 percent of the estimated 470 new researchers needed each year to maintain a stable research manpower pool nationally in microbiology and immunology, including clinical investigation of infectious diseases and clinical immunology.

FY 1982 Program Changes

This research plan has already spoken to the significance of infectious diseases and to the importance of a broadly based research strategy to prevent and treat infections due to microbes as diverse as viruses, bacteria, fungi and parasites. There are at least four major impediments that must be overcome by any research strategy to conquer infectious diseases. New initiatives and expansion of ongoing activities will be focused on these four major impediments to progress:

- The broad diversity among microbes that cause disease; with the corollary that additional diversity is generated through genetic mutability. This diversity complicates any strategy for prevention and treatment.

- The emergence of antibiotic or drug resistance among bacteria and other microbes which heretofore were readily treated--bacteria such as meningococci, gonococci, staphylococci, pneumococci and parasites such as those causing malaria. This troublesome problems of antibiotic resistance among bacteria is the result of their genetic ingenuity as manifested by persistent mutability and exchange of extrachromosomal DNA.

- The need to develop successful and safe antimicrobial compounds, particularly for viruses and parasites. There are virtually no cures for virus infections. And new research is needed to identify alternatives to the traditional antibiotics for the treatment of bacterial infections.

- The necessity to discover innovative ways to manipulate the immune system that represent a departure from conventional immunization procedures. One hundred years after Pasteur there are barely a dozen successful vaccines employed in the United States today. Any future strategy to combat infections will require new approaches to stimulate immunity.

A research program to lift these barriers that hinder the control of virus infections is outlined in the Virology Task Force report. The Advisory Council has abstracted 11 principal recommendations from this report, and

recommended that the NIAID investment in virus research be doubled by 1983. The Report goes further on the need for research related to the new partnership between virology and cellular and molecular biology. For example, recombinant DNA technology may yield for the first time a truly stable "master" vaccine strain of live influenza virus. Viruses are used as tools to probe the secrets of the cell and in the end this may be the most important legacy of research begun nearly a century ago. Viruses, frequently described as being on the edge of life, may yet prove to be the key to understanding the nature of life itself.

Molecular biology and recombinant DNA technology have presented new opportunities to investigate antibiotic resistance among bacteria as well as mechanisms of microbial virulence. Episomal (phages and plasmids) research has revealed that the genes which confer antibiotic resistance are carried on translocatable DNA elements and are capable of transposition from one bacterium to another even between species. Further research on episomes may lead to practial benefits, such as mechanisms to circumvent the development of antibiotic resistance.

Prior research plans have noted the expanding opportunities for research on the cellular and molecular biology of the immune system, including the complex interplay of events which regulates immune responsiveness. An overridding issue centers on the genetic control of immunity. Detailed investigations are needed of the genetic organization as well as the chemical nature of the gene products and the mechanisms by which these products regulate biologic and immunologic functions. The importance of genetics in the elucidation of immunological phenomena cannot be over emphasized. It provides a universal language through which biological events are inscribed and controlled.

New opportunities are developing to treat disease through modulation and regulation of immune responses. It is possible, for example, to eliminate selectively suppressor T cell activity, enhance tumor immunity and decrease tumor growth in animals. Such studies will undoubtedly have future pratical importance in elucidating the pathogenesis of autoimmune disorders in man and developing new treatment. Reagents that influence suppressor T cell activity, for example, might be beneficial for patients with lupus erythematosus, rheumatoid arthritis, malignancies, allergic diseases and possibly even infectious and parasitic diseases, such as leprosy and schistosomiasis, where inflammation has a major immunologic component.

Basic research is needed on the immunological and chemical mechanisms that are responsible for asthma and other allergic reactions as well as more clinical research on immunotherapy and other forms of treatment. Such studies will identify the critical processes where either immunological or pharmacological intervention may alleviate the allergic process. It is known, for example, that IgE antibodies to allergic substances (e.g.; ragweed) attach to specific chemical receptors on the surface of mast cells that are clustered in the "shock" organs where the allergic reactions most frequently occur--the nose, respiratory tract, gastrointestinal tract, and skin. The binding of IgE antibodies to mast cells releases vasopressor amines. There follows a cascade of chemical reactions involving a series of substances, including complement.

The end result of this chemical chain of events is the inflammation of allergies. Genetic influences hover over this allergic process in ways yet to be understood. Therefore, a better understanding of the genetics of the immune system and of allergic mechanisms is needed to improve the treatment and prevention of these disorders.

After review of the Asthma and Allergic Diseases Task Force Report, the Council recommended that the budget for this program be substantially increased by 1984. This recommendation was based on the Council's perception of the magnitude of the health problem and the current research opportunities. Furthermore, many medical schools lack programs in allergy and clinical immunology. As a result, the practice of these clinical specialties is not as widely dispersed as some other major medical specialties. Improvement of health care will in the end require that everyone have access to physicians thoroughly trained in allergic and immunologic diseases. Active and vigorous clinical research centers are the source and the training ground of these physicians.

The recently completed report of the Sexually Transmitted Diseases Study Group was reviewed by a special subcommittee of the Adivsory Council whose recommendations for research support and training were discussed by the full Council and adopted in modified form.

The opportunities identified by these 3 groups serve as a master blueprint of what is desirable to undertake. What is undertaken with limited resources will be quantitatively but not qualitatively curtailed.

In support of free ranging research in microbiology and immunology, the Institute will fund approximately 1500 research grants in FY 1980. This represents 74 percent of the total dollar outlay of extramural funds. An additional 17 percent will be devoted to program projects, centers and training.

Three practical issues bridge extramural and intramural areas: (1) facilities for testing experimental vaccines in volunteers; (2) facilities for the conduct of research involving hazardous microbes; and (3) risk assessment of recombinant DNA research. Although initial estimates for use of maximum containment (P4) facilities have been revised downwards and reflect changes in the Recombinant DNA Guidelines, the need for such containment has not been eliminated. New initatives in the third of these issues appear to be the most pressing and will be undertaken.

The Intramural Program, including reorganization of the Rocky Mountain Laboratories, provides new opportunities for research on viral persistence, the relation of microbial structure and function to virulence and pathogenesis, and the epidemiologic determinants that influence the occurrence of disease. It is not clear how to capitalize on these as well as to operate the new Ambulatory Care Research Facility without substantial staff increases.

Impact of Stabilizing Research Project Grants in 1981 and 1982

In accordance with the NIH plan to stabilize the funding of competing research project grants as its highest priority item, the NIAID was assigned a target of about 402 awards in FY 1981 and 420 awards in FY 1982. Both years are down from the 447 competing awards of 1980.

In FY 1981, the budget set aside for noncompeting and targeted numbers of competing grants, other noncompeting awards and mandatory items, effectively eliminated all competing awards for other research, centers and training. The decreases in numbers of awards from 1980 and 1981 are as follows: research centers, 35 percent; research career awards, 35 percent; and research contracts, 19 percent. The effect of the 1982 effort to maintain competing research project awards cannot be forecast until the budget process is complete.

Developing and maintaining a stronger science base means providing stable and predictable funding for a wide variety of research efforts in laboratory and clinical settings over a multi-year period. Stabilizing the science base is an initiative included in the DHHS Health Research Principles and its purpose and rationale are fully supported by the NIAID. However, we hasten to add that "science base", although mainly supported by research project grants (R01 and P01), also includes research centers, research career awards, research and development contracts, and intramural research. To concentrate any increased funding solely on competing research project grants for extended periods will have a detrimental effect on the other areas of the science base that provide a sound foundation for applied and developmental activities.

The primary impact of such funding decisions is to limit our ability to pursue clinical testing of new drugs and vaccines and to transfer new knowledge to the community. While advances will still be made in understanding the basic disease processes and "breakthroughs" will occur in some areas, it is our ability to apply these findings to the improvement of existing therapies and preventive measures that will not keep pace.

Summary of NIAID's Research Plan Review Session with the Director, NIH

The NIAID is an Institute burgeoning with scientific opportunity, but faces the dilemma of not having enough trained laboratory or clinical research manpower to take advantage of a technologic revolution that will have profound effects on medical practice in the 1980's. Neither does it have the flexibility of funding to allow opportunistic activities.

Research Advances and Opportunities

A presentation was provided on the utilization of new technologies that offer exciting examples of the application of basic biomedical research efforts.

- Hybridoma--The application of hybridoma cell culture, in combination with recombinant DNA technology, may make a practical malaria vaccine possible. Just two years ago this was an unlikely event; however, these techniques allow production of the specific, single malaria antigen that is known to stimulate human immunity.

- Recombinant DNA--The revised NIH Guidelines have permitted the use of recombinant DNA technology to better control and understand influenza virus. It should now be possible to develop a more effective live, attenuated virus vaccine rather than an influenza vaccine derived from killed viruses. The problem of genetically unstable viruses may be solved by basic research using these techniques.

- Immunotherapy--The possibilities for immunotherapy stem from the organization of the immune system--the T & B lymphocytes and their subtypes which have helper, suppressor or killer cell functions. Cells with these functions have specific surface antigens which identify them. Hybridoma produced antibody can be used to identify such cells, "sieve" them out of a mass population with an electronic cell counter or inactivate them or block recognition sites on the target organ cells.

  Application of these technologies to understand the pathogenesis of many diseases offers also the promise of mastery of the immune system. Mastery includes not only understanding the process of pathogenesis in many diseases but also rational, selective and precise manipulation of that system for intervention in a variety of clinical situations.

Stabilization of the Science Base

The proposal to stabilize NIH support of the science base, particularly as it would apply to predictable funding for research grants was discussed. Within a constrained budget, protection of competing research project grants would have a negative impact upon all other activities supported in the NIAID science base. In addition, Institute funded activities in clinical applications and technology transfer would be curtailed.

The nearly 80% of NIAID's extramural budget already in support of regular research project grants for FY 1980 will increase to about 84% in FY 1981. This is an unusually high proportion. The NIAID would use additional funding to take advantage of new opportunities in areas of clinical application and technology transfer.

Training/Manpower Development

Within the context of balancing the competing priorities of expanding science and the support of training, the following were discussed:

- Clinical training--In the Institute's view, the level of trained scientists in allergy, infectious diseases, and clinical immunology is much lower than in some other fields. Also, the geographical distribution is uneven. NIAID would like to establish centers of research excellence in order to rectify these problems. It was noted with concern that at the current trend, the number of NIAID clinical trainees would be reduced by 50% in 10 years. But perhaps a more perplexing problem is how to go about stabilizing the current level of these trainees even though this level is considered less than optimal.

- Postdoctoral training--The NIAID Advisory Council devoted one of its meetings last year to a discussion on NIH training policy and programs. The findings of the Council were contained in a recent report to the Associate Director for Extramural Research and Training, NIH. A number of issues were discussed that arose from this report. NIAID estimates that 600 postdoctorals need to be trained per year in order to maintain a steady state of available manpower. Currently, only 300 to 400 trainees (with 100 trainees graduating annually) are being supported in clinical and basic science areas. A final report on the Microbiology Manpower Survey by the ASM is expected in the fall. This should help to estimate more accurately the size of the manpower pool to which NIAID training contributes.

Major Civil Rights and Affirmative Action Initiatives

During FY 1979, NIAID continued its support of the MARC, MBS and Cooperative Education Programs. An assessment is being conducted of supervisory and management practices to identify EEO training needs. The EEO Plan has been updated in accordance with EEOC Guidelines. The NIAID Minority Recruitment Program for undergraduate and first year graduate students, initiated last summer was quite successful, and plans call for increasing the size of this program in 1980.

Task Force Recommendations

Over the past year, the NIAID Advisory Council has been reviewing the reports of the Virology Task Force and the Asthma and Other Allergic Diseases Task Force, and has presented the Institute with a number of recommendations in these research areas.

- Virology--Over the next five years, the Council recommended that the NIAID expand its support of research in 10 specific areas, as well as in training.

- Asthma and Other Allergic Diseases--Recommendations were made to increase research and training efforts in 12 specific areas. The sequence of events in allergic reactions is generally understood and the major opportunities now are for new forms of treatment, including immunotherapy and pharmacological intervention. As one response to these recommendations, NIAID plans to increase the numbers of asthma and allergic disease centers and to establish these centers in medical school departments where relevant specialties are located.

Consensus Development

- In October 1979, NIAID sponsored a conference to review information available on the use of amantadine hydrochloride in the treatment and prevention of influenza A. Results of the successful conference were published in the Journal of the American Medical Association and in Science, both on November 30, 1979.

- Future possibilities for consensus projects include a conference planned for April on treatment of bacterial endocarditis, to be held in conjunction with NHLBI and the American Heart Association. There are also plans for a state-of-the-art workshop on urinary tract infections in pregnancy.

Intramural Program Issues

- Increased support for exciting new technologies described previously also pertains to the intramural research programs. However, the increase in the intramural budget for FY 1980 is 5.7%, with a possible 3.3% increase in FY 1981. With inflation, this represents an actual decrease in support. The Institute is concerned that if this situation persists over a few years, programmatic flexibility will greatly decrease.

- Rocky Mountain Laboratory--Recruitment is going well and the new laboratories of persistant viral diseases (LPVD) and bacterial pathogenesis (LMSF) are beginning to take shape.

- ACRF--Plans call for expanding the outpatient portion of the allergy program and clinical tropical medicine. To the maximum extent possible, existing personnel will be redistributed; however, not all of the planned program expansions can be addressed by reprogramming resources. Additional resources would be required to handle the anticipated increase in patients.

- Containment facilities--Certain kinds of research cannot be undertaken at this time because of the lack of proper containment facilities. This research includes initiating studies on microbial virulence

requested by NIAID advisory groups, examining recently received specimens from Africa, performing risk assessment studies mandated by the Recombinant Advisory Committee including the use of wild type organisms, and undertaking hepatitis and other such vaccine studies which would require using high containment laboratory facilities.

The National Advisory Allergy and Infectious Diseases Council members, Drs. McDevitt and Stollerman, participated in the review session. Their insight contributed immensely to the discussion of many of the issues.

Chapter 4

NATIONAL INSTITUTE OF ARTHRITIS, METABOLISM AND DIGESTIVE DISEASES

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Chapter 4

NATIONAL INSTITUTE OF ARTHRITIS, METABOLISM, AND DIGESTIVE DISEASES

Director's Preface

Significance of the Health Problem

The programs of the National Institute of Arthritis, Metabolism, and Digestive Diseases encompass a wide range of common and important chronic diseases, including arthritis and related musculoskeletal and skin diseases; diabetes mellitus, cystic fibrosis and other metabolic and endocrine disorders; digestive and nutritional disorders; and diseases of the kidney, urinary tract and blood. These diseases affect millions of Americans of all ages and both sexes and all ethnic groups and strata of society, exacting a devastating toll of chronic disabilities, pain, financial depletion, and premature deaths.

As control of the major killer diseases improves and the average age of the U.S. population increases, the number of people at risk for these chronic, disabling diseases is expected to increase sharply, further taxing the nation's personal and medical resources. At the same time, there is a great disparity between the magnitude of the problems and costs generated by these diseases and the resources directed toward improving our ability to combat them. Unless our commitment to preventing and controlling chronic diseases becomes more commensurate with their impact, morbidity and costs are likely to continue upward.

Program Strategy

While advances have been made in the diagnosis and treatment of many of the diseases for which NIAMDD is responsible, their causes for the most part remain either poorly understood or unknown. It is therefore the Institute's foremost priority to foster fundamental and clinical investigator-initiated research on life processes in health and disease and on the etiology, diagnosis, and treatment of the diseases within its mandate. Scientists in every discipline cooperate in this effort to understand the complex interplay of factors involved in the natural history and management of chronic disease. As scientific opportunities emerge, the Institute also supports applied and developmental activities to meet the need for more effective and safe medical care, as well as continuing efforts to transfer new knowledge to the medical community and the public.

Goals

The Institute's primary goal is to improve the ability to prevent, diagnose and treat a wide variety of disease entities and conditions through biomedical research and research training. Continued progress in attaining new scientific knowledge will alleviate human suffering and contribute to reducing the direct and indirect costs of medical care.

FY 1981 and FY 1982 Program Changes

In general, the planning assumptions for FY 1981 do not allow for major new initiatives and will result in substantial deferral, reduction, or elimination of research activities.

Arthritis, Musculoskeletal, and Skin Diseases

Arthritis

Several important new advances in arthritis research suggest the potential for major breakthroughs in ameliorating or controlling the progress of this disease. One of the most exciting of these advances relates to the discovery of genetic markers (histocompatibility antigens) in body tissues of individuals suffering from a number of common types of arthritis, including rheumatoid arthritis. By providing a means of identifying individuals at risk for specific types of arthritis, discovery of these markers makes possible more effective use of therapeutic agents to prevent the destructive effects of rheumatic diseases. Special new research activities, some in collaboration with NIAID, are planned in immunogenetics and regulation of the immune system to exploit this research advance.

Recent research findings have also implicated infectious agents--both viruses and certain strains of bacteria--as one of several environmental factors which could activate or "trigger" an individual's existing predisposition to rheumatic disease. Future research will be aimed at further isolation of these infectious agents and refinement of techniques for identifying their modus operandi.

To improve therapy of rheumatic diseases, researchers will be focusing on the action of anti-inflammatory agents and various medications which suppress the body's immune response. In addition, investigators will evaluate the effectiveness of radiation synovectomy as an alternative to surgery in some forms of arthritis, and of plasmapheresis in providing symptomatic relief to patients with severe rheumatoid arthritis.

The network of coordinated clinical trials in arthritis will supplement its ongoing studies with new emphasis on therapeutic agents in scleroderma and polyarteritis.

The multipurpose arthritis center (MAC) program has redesigned its goals to promote greater substantive and administrative efficiency. However, even with the modest increase in funding planned for FY 1981, rising costs are expected to result in severe cutbacks in either the scope or the number of MAC's.

Musculoskeletal Diseases

It has been estimated that nearly half a million fractures are caused each year by osteoporosis. With NIAMDD support, investigators have identified a number of alternative treatment schemes for this condition, most notably calcium supplementation, administration of therapeutic vitamin D and its biologically active metabolites, and administration of fluorides. It is one of the Institute's highest priorities to initiate, probably in FY 1982, a

clinical trial to evaluate the effectiveness of combinations of these therapeutic modalities for slowing and possibly arresting or reversing the progress of osteoporosis.

Research will continue on the use of electromagnetic stimulation to promote healing of non-union bone fractures, already found to be successful in as many as 80 percent of patients studied. Of high priority are improvement of artificial implants for replacement of irreparably damaged arthritic joints, and identification of the causes of osteogenesis imperfecta and other disorders of bone structure. Finally, this program also plans to foster a multidisciplinary approach to the understanding and treatment of back diseases, with emphasis on the extremely common idiopathic forms of these diseases.

Skin Diseases

In this area, the report mandated by Congress, "Analysis of Needs and Priorities for Research in Dermatology," is expected to stimulate a substantial increase in applications for research in diseases such as psoriasis, pigmentation disorders, acne, and atopic dermatitis, and in basic studies of structure, function, and metabolism of skin.

The Institute enthusiastically supports the initiation of a clinical trial on the efficacy and long-term safety of oral retinoids in treating certain of the most severe recalcitrant cases of acne, and congenital ichthyosis ("alligator skin"), but the trial will probably not be initiated before FY 1983 because of funding restraints. In limited trials. one of the oral retinoids, 13-cis-retinoic acid, has been shown to be effective in decreasing human sebum production by as much as 90 percent without serious side effects.

Special attention will be given, in collaboration with NIAID, to supporting the emerging field of immunodermatology, particularly regarding atopic and contact dermatitis. Two other activities which the Institute expects to maintain are a consortial effort in vitiligo which was recommended by Congress, and a clinical trial of PUVA (a combination of oral psoralens and long-wave ultraviolet irradiation). If sufficient funds are available, this trial will continue to monitor any long-term ill effects of treatment with PUVA--widely used for severe, intractable psoriasis--and will begin to test the efficacy and safety of this treatment for vitiligo.

Diabetes, Endocrinology, and Metabolic Diseases

Diabetes

A number of research advances on the etiology, aberrant metabolism, and management of diabetes have created a great deal of activity in this program. Researchers have demonstrated that insulin-producing cells both in tissue culture and in experimental animals, as well as in man, can be infected by certain kinds of viruses. Further studies of the association of genetic factors and viral infection will be encouraged, with the ultimate aim of preventing diabetes in genetically susceptible individuals. If given additional resources, this program would also seek new information on the etiology, genetic and environmental determinants, and risk factors of both insulin-dependent and non-insulin-dependent diabetes, through studies of the immunogenetic and demographic characteristics of individuals in diverse populations.

To improve clinical management of diabetes, this program will foster continued progress in the development of a new generation of technologies for automatic administration of insulin at programmed intervals to diabetic patients. These new technologies, which have the potential for restoring near-normal metabolic homeostasis to insulin dependent diabetics, will be used in studies related to the development of diabetic complications. A major clinical trial will be ready for initiation in FY 1982 but will probably be deferred because of funding limitations. It will focus on the relationship between the degree or "strictness" of control of blood glucose and metabolic homeostasis and the development of diabetic complications. In an attempt to resolve one of the most controversial issues in diabetic research, this clinical trial would compare the effect of customary diabetic management with an intensive therapeutic program designed to maintain near-normal blood sugar levels.

Recently, the successful transplantation of pancreatic islet cells in experimental animals produced a reversal of diabetes in the recipient animals. Funds will unfortunately be too scarce to pursue adequately the intriguing, though tenuous, possibility of transplantation of insulin-producing cells into human diabetics. Resource constraints will also preclude optimal funding of Diabetes Research and Training Centers for the foreseeable future.

Endocrinology

This program emphasizes fundamental research on various aspects of normal biological functions and the manner in which these functions are altered in specific endocrine-related diseases. A modest amount of new research is planned in regulation of endocrine cell growth and differentiation and hormone biosynthesis and secretion. Intensified study will be encouraged on the function of hormone receptors on cell surfaces and on immunogenetic mechanisms of endocrine disease. High priority will be given to research aimed at isolating and characterizing new hormonal factors, synthesizing known hormones by chemical or biological means, or identifying new agents to augment or inhibit the action of hormones.

Following a FY 1981 assessment, the National Pituitary Agency may be modified to become a national hormone program for production and distribution of additional hormones, antibodies, and antisera essential for endocrinology research. To be deferred for lack of funds is a broad program of support for specialized research resources needed to greatly enhance research potential in endocrinology.

Metabolic Diseases

This program emphasizes: research on fundamental mechanisms underlying the regulation of cellular metabolism, including factors regulating gene expression in metabolic diseases and in healthy states; chromosome localization of structural genes; and the role of enzyme inhibitors in disease treatment. New research activities are planned on various genetically determined inborn errors of metabolism. Also of vital importance in this area are studies of enzyme replacement therapy for various inborn errors of metabolism.

A major focus of this program is cystic fibrosis (CF). If resources permit, this program would expand further its multidisciplinary programs of research into the causes and nature of CF and its associated complications.

Efforts will be made to develop effective tests for detection of the heterozygous carrier state of this disease and for prenatal diagnosis of potentially homozygous fetuses. Following preliminary studies in 1981, a multicenter clinical study is scheduled to begin (but likely to be deferred) to improve understanding of the disturbed gastrointestinal function, digestive enzyme activity, and other nutrition-related aspects of CF. Because of funding constraints, however, plans to initiate a research resources program to improve the availability of CF tissue samples will have to be deferred at least until FY 1982.

Digestive Diseases and Nutrition

Digestive Diseases

A variety of new approaches have been planned in response to recommendations of the National Commission on Digestive Diseases, but most will probably be deferred until FY 1982 or later because of insufficient funds. One exception is the modest, initial development of a National Digestive Diseases Education and Information Clearinghouse, the Commission's leading recommendation.

Already delayed because of resource limitations is a controlled clinical trial on chronic active hepatitis, now planned to begin either in FY 1982 or later. Asymptomatic chronic active hepatitis (CAH) is a relatively severe, progressive type of hepatitis usually with a poor prognosis. The factors responsible for causing or escalating this disease have not been identified, and there is uncertainty concerning effective treatment approaches. This trial would attempt to determine the proper treatment of asymptomatic CAH, and particularly whether treatment with corticosteroids is indicated.

A controlled, multi-center clinical trial on upper gastrointestinal hemorrhage has also been planned by the Digestive Diseases Program for initiation in FY 1981, although delay of this start date seems probable. This trial would evaluate the efficacy and safety of two endoscopically delivered techniques, bipolar electrocoagulation and argon laser photocoagulation, both regarded as promising non-surgical therapies for bleeding gastric, duodenal, and stomal ulcers. A consensus development conference on the subject in the summer of 1980 will precede such a trial.

Cirrhosis of the liver is the sixth leading cause of death from disease. An intensive initiative is therefore planned to improve understanding of the immunogenetic mechanisms and the effect of drugs and other factors which cause adverse reactions in the liver. Improvement of the accuracy of methods used in identifying individuals susceptible to such adverse reactions will also be stressed.

Collaborative projects on pancreatic diseases will be given high priority, particularly regarding the roles of risk factors, such as alcohol abuse, gallstones, trauma, and drug usage. Additional research will also be encouraged on neuroendocrine control of the digestive system.

Nutrition

The Institute's Nutrition Program is actively participating in the innovative cooperative NIH initiative on clinical nutrition which has given rise to the Clinical Nutrition Research Units. These units--three of which are

already supported by this program--are expected to increase nutrition research in medical schools and involve a larger number of investigators in medical training in nutrition. In FY 1982, high priority will be given to stimulating research on improved nutrition of hospitalized patients and to establishing a limited number of additional Clinical Nutrition Research Units.

This Nutrition program will also be prepared in either FY 1981 or 1982, although initiation might occur even later, to begin a multi-center clinical trial to evaluate the efficacy of total parenteral nutrition, defined enteric formula diets, and other modes of nutritional support in patients with inflammatory bowel disease or short bowel syndrome. The results of this study would help to resolve uncertainty concerning the optimal therapeutic approach for reducing morbidity and mortality in this patient group. This study would also provide controlled data for evaluating alternative nutritional support systems in this and other medical and surgical conditions.

Other new initiatives in this program, including a recent program announcement on obesity, have attracted increased numbers of high-quality applications. A new departure is planned in this area in FY 1982 to identify pathophysiologic and etiologic mechanisms of specific types of obesity and to evaluate new and more effective modalities of therapy and prevention.

Kidney, Urologic, and Blood Diseases

Kidney and Urologic Diseases

This program will concentrate during the next two years in three areas having a high potential for prevention of kidney disease or for improved patient rehabilitation at lower overall cost. The first new initiative, scheduled for FY 1982, would intensify experimental and epidemiologic studies on the role of commonly prescribed drugs and environmental agents in producing kidney toxicity and subsequent kidney disease. Second, the Institute plans to develop a cross-disciplinary research program on immunologic mechanisms and the causation of renal disease. Glomerulonephritis, the primary disease to be studied in this program, is a major contributor to mortality, morbidity, and the cost of illness in the U.S. and is responsible for a large proportion of the loss of renal function requiring management by dialysis and/or renal transplantation. The pathogenesis of glomerulonephritis is largely unknown, however, and no specific or effective treatment has been developed. Given sufficient funds, a clinical trial on the natural history and therapy of glomerulonephritis would begin in FY 1982.

The third approach will involve redirection of three ongoing studies on dialysis therapy. One study, a Congressionally-mandated evaluation of the feasibility and safety of dialyzer reprocessing and reuse, may call for clinical comparisons in controlled studies by FY 1981. Also by FY 1981, a limited evaluation of continuous ambulatory peritoneal dialysis should be ready for moderate expansion. A third project, the National Cooperative Dialysis Study, should have progressed to the stage of data analysis by that time; guidelines developed as a result of this analysis should help in defining the lower limits of costly hemodialysis therapy necessary to keep patients rehabilitated and free of complications of dialysis treatment.

Specialized Centers of Research in Urolithiasis, recommended by Congress, should continue at a relatively constant rate of support in FY 1981 and 1982. Studies of such high priority areas of Congressional concern as benign prostatic hyperplasia, which affects the majority of men over age 55, will continue at a lower than optimal level. In general, most aspects of this program will be deprived of the opportunity for much needed expansion.

Blood Diseases

A variety of new accomplishments in blood diseases research deserve additional impetus. One area of high Institute priority and special Congressional concern is research on the cause of and therapy for Cooley's anemia. A prime focus for improving therapy of this disease is efforts to develop new iron chelating drugs for correcting ultimately fatal iron overload, which occurs as a result of multiple therapeutic blood transfusions. Funding limitations will, however, preclude toxicity trials of a potentially successful chelating agent (EDBHPA), now under pharmacologic study.

Bone marrow transplantation has increased the survival rate of patients with blood diseases. However, because histocompatability boundaries complicate graft acceptance and severely limit the use of this surgical technique, much additional research is needed in this area, and the Institute plans a major collaborative effort.

Recent therapeutic advances in patients with acute porphyria highlight the need for additional research in hematology, particularly on the etiology and treatment of abnormal heme synthesis. Major research efforts are also needed on the characterization of early events in bone marrow stem cell differentiation and other normal and pathologic bone marrow activity. Similarly, at the interface of nutrition and hematology, more studies are needed on the nutritional anemias; other investigations must explore the induction of anemia by toxic environmental agents.

Manpower Development and Training

Assurance that an adequate pool of talented investigators is available to assure continued progress in the biomedical sciences is a high Institute priority. The Institute is convinced that the most effective way to accomplish this goal is by formulating a research manpower development program that will provide a graduated spectrum of research support mechanisms designed to fit the needs of motivated future investigators. Several recently initiated mechanisms, such as the New Investigator Research Award, the Clinical Investigator Award, the NRSA Senior Fellowship, and the Special Emphasis Research Career Award should contribute markedly to the Institute's ability to attract talented scientists and prepare them for research careers. The effectiveness of these programs will be monitored. The Institute also plans to encourage the development of short-term training programs to enable medical students to gain experience in research during the summer.

Unfortunately, despite the soundness of the programs offered, a thriving manpower development program is all but impossible to maintain in these times of severe cutbacks. This problem will be most evident for this program in FY 1981 when, given the budget allocations allowed for training, NIAMDD will be unable to fund any new or competing NRSA training awards.

Summary of NIAMDD's Research Plan Review Session with the Director, NIH

Program Overview

A number of factors which complicate the Institute's ability to respond to the concerns and directives of the Congress, the scientific community, and the public were reviewed. NIAMDD's program responsibilities are very broad, including much of internal medicine and several subspecialties of surgery. The Institute therefore interacts with a diverse array of constituency groups and voluntary associations as well as a number of Commissions and Advisory Boards. Not only is the Institute's Congressional mandate complex, but the appropriations subcommittees customarily designate a number of programs for special emphasis. In FY 1980, for example, the Senate recommended increased emphasis in all major Institute programs, and particularly training, while the House directed that high priority be given to funding additional research project grants. To respond to these directives in FY 1980, the Institute plans to increase support for research grants and training, and must consequently selectively reduce support for center grants and contracts.

For the past two years, the Institute has made a special effort to involve the National Advisory Council in the deliberations which must occur as a result of these directives. This involvement has resulted in the research community being better informed about the nature of and reasons for shifts in Institute resources.

Stabilization of the Science Base

Most of the discussion centered around the recent proposal to stabilize NIH support of the science base, and in particular to provide stable and predictable funding for research project grants. NIAMDD would attempt to stabilize the science base by fixing the number of competing awards for research project grants at the FY 1981 level of 763. For each successive year support for competing awards would be increased by 8%, and by a somewhat larger amount for noncompeting awards, to offset inflation.

The Institute strongly recommended that research career awards be made an integral part of stabilized extramural support, and suggested that NRSA training also be considered for inclusion. Serious reservations were expressed about the effect of any mandatory stabilization of research project grants upon other support mechanisms, such as contract activities, centers and intramural research. One program area which may be adversely effected first is that of clinical nutrition research centers, which have only recently been initiated and for which an expedited establishment of three centers per year has been planned.

Centers

The status of center grant support within the Institute was discussed, and the continuing effort by NIAMDD to emphasize core support as a principal means of funding centers. The gradual conversion of SCORs to core centers, and the recent introduction of core support as an allowable component of the

Multipurpose Arthritis Centers are steps toward that goal. In addition, the MACs have been encouraged to seek other sources of support for those training and demonstration efforts which have become successful. A related effort is being made to include a significant clinical element in each class of center grants.

Major Civil Rights and Affirmative Action Initiatives

The Institute has established two important inter-Institute agreements in the past year in the area of equal employment opportunity. One with the Division of Research Resources provides some funding for the DRR's Minority Biomedical Support Program. Similarly an agreement with NIGMS provides some funding for the Minority Access to Research Careers Program. The Institute has also expanded its offering of courses for intramural employees.

Follow-up on Evaluation Review Session

- The assessment of the impact of the Cystic Fibrosis Conference on research in that disease area is in progress. In the Institute's view, the conference was productive, serving to identify needed research approaches and to heighten investigator awareness of needs and opportunities in CF research. Some stimulation of CF-related grant applications has occurred as a result of recent Program Announcements and the Conference, but it is not yet known if these measures have drawn new investigators, especially from other disciplines, into the field.

- The Institute is currently using several methods to assess the results of pilot and feasibility projects funded through the Diabetes Research and Training Centers and the Multipurpose Arthritis Centers. These centers programs are analyzing the proportion of such projects which become the basis for traditional NIH research grant awards or which result in the presentation of scientific papers at meetings of professional societies. The Institute is also examining the role of pilot and feasibility funding in the support of new investigators and the encouragement of multi-purpose research efforts. Preliminary analyses of the results of some of these assessments suggest that pilot and feasibility projects are an active and productive part of both classes of centers, yielding significant numbers of funded research projects, scientific publications, and new investigators.

Mrs. Grace Kraft and Dr. Paul Lacy attended the meeting on behalf of the National Arthritis, Metabolism and Digestive Diseases Advisory Council.

Chapter 5

NATIONAL CANCER INSTITUTE

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Chapter 5

NATIONAL CANCER INSTITUTE

Director's Preface

Significance of the Health Problem

Cancer is the second most common cause of death in the United States. In the next year approximately 400,000 people will die of cancer, and almost twice as many new cases will be diagnosed. Among Americans, it is the most feared disease. The impact of cancer is felt in lives cut short, in income lost by working lives ended prematurely, in the costs of treatment and care, and in the physical and emotional pain the disease brings.

Although cancer is most often a disease of older ages (in recent years between 50 and 55 percent of new cancer cases were in persons over 65), the average person who dies of cancer still loses over 15 years of life. Among men, where cancer occurs on the average a little later in life than in women, about 14 years of life are lost to each cancer death, compared to slightly more than 18 years for women. The cancers of children and young adults, of course, lead to the greatest number of years of life lost.

Trends in mortality in cancer are different for different ages. The incidence of cancer (age-race-sex taken into account) has been increasing at about one to two percent per year in the 1970's. Mortality increases have been smaller, about 0.3 percent per year. The difference between incidence and mortality reflects improvements in survival, particularly in children and young adults. The age-specific mortality trends show declines in the younger age groups, relative stability in the middle age groups, and increases in the older age groups.

Since over 700,000 new cases of cancer are diagnosed annually in the U.S., more than seven million persons are affected each decade. Based on current incidence and survival rates, there should be over four million former cancer patients alive in 1984. Thus, the United States may anticipate an increasing need for expert medical care, nursing care, aftercare facilities, rehabilitation programs, and other community and family services required by the increasing number of people who develop and survive cancer.

Program Strategy

It is difficult to set priorities for support of research in the various fields that compete for limited funds. Invariably, attempts to do so have encountered reluctance on the part of scientists to make qualitative judgments as to the relative scientific importance of the different but interrelated areas of research. Nevertheless, pressure to assign priorities and to rank activities according to their relative importance is increasing. Arguments are made that research is undertaken in the service of humanity and that research priorities should be based on the potential beneficial application of

research results to recognized societal as well as scientific problems. It is currently desired that NCI increase the priority for research aimed at the prevention of cancer. At the same time, humanitarian considerations dictate continuing a high priority for research aimed at improved treatment of individuals who now have or will have cancer.

The following tenets serve as the basis for the program strategy of the National Cancer Program:

1. Much of the knowledge crucial to the solution of cancer and other scientific problems is "fundamental" knowledge, i.e., derived from basic research.

2. While the importance of fundamental research is a given, it is recognized that our mission requires us to plan and conduct a program in which applied research and developmental activities are also conducted where sufficient knowledge exists.

3. Cancer is a world-wide problem, and much can be learned from the experiences of other countries and the results of their research efforts. This requires the exchange of information among investigators throughout the world.

4. It is important to develop a coordinated national program and to utilize all available resources, while seeking to mimimize unnecessary duplication of efforts conducted by other participants in the National Cancer Program.

5. It is important to foster the timely and practical application of research findings through appropriate education/demonstration programs.

Translating these tenets into a strategy for each of the three program components (Research, Control, and Resource Development) results in the following:

Research Strategy--Ideally, prevention is ultimately the most effective approach to the control of cancer. However, while knowledge is being sought to develop the means to prevent cancer, new cases of cancer will continue to occur. Hence, cancer research must continue to be directed toward the management of the disease as well as its prevention. For both the prevention and treatment of cancer, however, further knowledge of the control of cell growth and differentiation must be sought through basic as well as applied research.

Cancer Control Strategy--It is through the application of research results that the control of cancer will ultimately be achieved. Hence, the Cancer Control Program is designed to aid in the dissemination and application of new knowledge. The program is concerned with all aspects of cancer--prevention, screening, diagnosis, treatment, continuing care and rehabilitation. Emphasis is placed on educating and informing health practitioners and the general public. The overall goal of the Cancer Control Program is to demonstrate proven and practical applications of research findings and to minimize the time required for their application to health care.

Resource Development Strategy--The training of needed manpower, construction of research facilities, and the development of centers of scientific and clinical excellence are part of the overall strategy, with a view toward the prevention or alleviation of critical shortages or deficiencies.

Goals

The goal of the National Cancer Institute is to develop the means for eliminating or controlling cancer. In order to achieve this, the NCI seeks to produce new knowledge through a balanced effort encompassing a spectrum of fundamental and applied research; to promote the widest possible utilization of current knowledge through demonstrations and educational activities in cancer control; and, through the development of needed resources such as trained manpower and specialized facilities, to assure continuing capability to carry out these activities.

FY 1981 Program Changes

Major Activities to be Initiated in FY 1981

In cancer biology research, studies concerning the basic mechanisms of tumor immunity will be emphasized. Ultrasound probes will be evaluated intensively in detection and diagnosis research. If sufficient progress is made, evaluation of electronic x-ray image recorders will begin. Biological markers for breast cancer will be explored, utilizing available sera from breast cancer patients, as well as benign and normal controls.

In treatment research, clinical trials using available high-energy neutron therapy equipment, the deuterium-tritium (DT) generator and the M. D. Anderson cyclotron, will be initiated. Estrogen receptor determinations will become routine tests in the treatment of breast cancer, and new protocols based on this test will be initiated. The Biological Response Modifiers Program will initiate clinical trials with some 50-billion units of three types of interferon--lymphoblastoid, fibroblast, and leukocyte--in signal tumors. Other biological response modifers, such as thymosin, will reach the stage of clinical testing. Development of other products, such as lymphokines and tumor antigens, will be initiated.

In the Drug Development Program, an *in vitro* system using a human stem cell cloning assay will be evaluated as a screening tool to identify those compounds most likely to be effective. This effort will be carried out in addition to the *in vivo* systems, such as the L1210 and human tumor xenografts (including the kidney capsule), which are currently being evaluated.

The Diet, Nutrition, and Cancer Program will initiate a grant program on the role of alcohol in the causation of cancer, with emphasis on epidemiology and basic research.

The Smoking and Health Program will initiate further surveys to determine the current prevalence of smoking among the general population, with emphasis on teenagers, women, nonwhites and blue collar workers, and to determine the behavior patterns of smokers, i.e., inhalation patterns, brand usage and

switching, and alcohol consumption. The new surveys are unique in that they concern high risk populations and low tar cigarettes.

In the Organ Site Program, activities to be initiated include:

Large Bowel Cancer Project--Establishment of a serum bank as a resource for standardization of immunologial assays; development of methodology for cell separation in normal tissue and colon cancer, including *in vitro* cultivation of normal colon epithelium; development of a colon tumor model with high specificity for liver metastasis; and the improvement of mutagen assays, including the isolation and identification of the mutagens per se.

Bladder Cancer Project--A Phase III trial for patients with clinically localized invasive bladder carcinoma who are not candidates for surgery; a comparison of radiation therapy alone with radiation therapy plus cis-diaminodichloroplatinum; and the development of a new program to study the psychosocial environment of patients in whom bladder cancer has recently been diagnosed or in patients following cystectomy.

Pancreatic Cancer Project--Extension of a series of Phase I and II pilot studies to evaluate the effectiveness of single and combined chemotherapeutic agents, combined modality therapy, and intraoperative radiation therapy in pancreatic cancer patients.

Prostatic Cancer Project--New clinical trials to evaluate chemotherapeutic agents as long-term adjuvants in patients with earlier stages of disease; and expansion of detection and diagnosis research, particularly in developing methods for earlier detection of localized disease.

The Cancer Control Program will conduct a major reassessment of the nation's cancer control needs, resources, and operations, including management analysis of the patient referral mechanisms and relative effectiveness of Centers' Outreach, Clinical Oncology Programs, Community-Based Cancer Control Programs, Clinical Cooperative Groups, and the various treatment networks.

A new training program in veterinary pathology will be initiated as part of the manpower development effort.

New initiatives in the Cancer Communications Program will result in more reports which will describe the state-of-the-art in specific areas of cancer research (immunology, detection, diagnosis, etc.). A major public survey will be conducted to determine public knowledge concerning cancer. A public awareness program will be initiated to include information concerning the validity of animal testing. Prevention-related activities will increase, particularly those aimed at high-risk populations.

Major Initiatives to be Maintained in FY 1981

Cause and prevention research will continue to emphasize studies using hybridoma technology, and on herpes virus model systems, chemoprevention, carcinogenic hazards of medical treatments, and the contribution of specific nutritional factors to the prevention and causation of cancer.

Planning for a program of low-level ionizing radiation research, to complement but not to replace ongoing research in other areas, is currently being pursued in the National Cancer Institute.

The major elements of the planned NCI program include the following:

- Fundamental studies regarding radiation dosage and biological effects; and how effects are modified by distribution of dose over time, by physiological conditions, and by other biological response modifiers.
- Efforts to identify, develop, and apply methods of protecting humans and minimizing their exposures to deleterious irradiation.
- Efforts to further develop research technology, methodology, and results assessment.
- Research to define both biological and environmental pathways for radionuclides in our ecosystem.
- Resources development relating to skilled scientists, information systems and educational activities.

In treatment research, construction of the facilities to house the equipment of the High-Energy Neutron Therapy Program will continue. Combined modality approaches, new and modified surgical procedures (i.e., limb-sparing operations and cytoreductive surgery), and drug development will continue to be emphasized.

The Diet, Nutrition, and Cancer Program will continue to fund several Clinical Research Nutrition Units, study the role of dietary fats as a cause of cancer, support increased research training in nutrition and cancer, and inform the public about factors in diet and nutrition as related to cancer prevention.

The Smoking and Helth Program will continue studies on smoking cessation in industrial populations, especially in those workers who may be exposed to occupational carcinogens.

Large bowel cancer studies will be maintained as a multidisciplinary program aimed at defining the metabolism and mechanisms of action of colon carcinogens and of promoters, modifiers, and inhibitors of colon cancer. Research is being continued in areas that emphasize causation of large bowel cancer, identification of high-risk individuals, and the diagnosis, pharmacological control, prevention, and treatment of colon cancer.

In the Bladder Cancer Project continued emphasis will be placed on understanding tumor initiation and promotion, developing markers of preneoplastic change and early tumor development, identifying high risk populations, seeking means for systemic and intravesicular chemotherapy of superficial bladder lesions, conducting clinical studies of methods to prevent recurring bladder tumors, and developing improved techniques for evaluating the sensitivity of tumors of individual patients to chemotherapeutic agents.

In the Pancreatic Cancer Project studies will be maintained to assess the significance of occupational exposure to carcinogens, alcohol consumption, and diet in the etiology of pancreatic cancer. Epidemiologic information on pancreatic cancer is being emphasized, and several case-control studies examining socioeconomic, environmental, and dietary factors will continue, with the aim of identifying groups at high risk for the disease. Early diagnosis continues to be an important research area, with an emphasis on tumor markers, laparoscopy, scanning techniques, ultrasonography, radioisotope uptake studies, and immunologic studies.

In the Prostatic Cancer Project research to characterize animal as well as *in vitro* models will continue. Studies of the epidemiology and etiology of prostate cancer will emphasize genetic and endocrine risk factors, with continuing attention to the possible role which viral particles play in prostate cancer. Detection and diagnosis research will maintain emphasis on characterization of receptor proteins, as well as on the search for new antigen markers for the diagnosis and staging of prostatic cancer.

Resource development projects will continue to provide training of manpower for cancer research and for clinical oncology. Studies to evaluate the effectiveness of cancer education will be maintained and should result in the refinement of criteria for cancer education in medical and dental graduate training programs and in the training of other health professionals, such as nurses, physician assistants, and dental hygienists, and in the development of an information gathering system to permit accurate reporting on all aspects of the educational activities being supported in grantee institutions.

The Cancer Centers Program will continue to foster multidisciplinary research through support of developmental research costs, shared resources, and central services. Efforts will be directed toward consolidation and integration of the various program components rather than overall expansion. Prevention programs, however, will continue to expand in a number of cancer centers. As part of this effort, increased support for epidemiology, including the direct support of salaries for senior epidemiologists to head these programs, will continue.

Major Activities to be Reduced in FY 1981

Budget constraints for FY 1981 will necessitate a reduction in funds to support Research and Development Contracts which include the NCI contribution to the National Toxicology Program. As a result, the anticipated number of chemicals to be tested will be reduced.

Thermography studies will be dropped, at least until further research is indicated by new data on the efficacy of this approach in tumor detection.

In the Large Bowel Cancer Project there will be a de-emphasis on histological and cell kinetic studies, pending the development of better methods for cell separation. Immunological studies related to diagnostic markers and therapy will also be cut back until there is more definitive information from ongoing basic immunobiological studies. Studies of high dose methotrexate with leucovorin rescue, which have been ineffective thus far, will be terminated.

In the Bladder Cancer Project, efforts in the area of cell-mediated immunity will be decreased until more information has been obtained about the basic mechanisms involved.

Cancer Control programs to be phased down include the Breast Cancer and Cervical Cancer Demonstration Programs, since several of the cervical cancer projects will be completed and the breast cancer projects are moving into follow-up phases.

In the area of Resource Development, support for some manpower development programs and activities, i.e., Research Career Program, Clinical Education Program, cooperative clinical research, individual and institutional training, will be reduced. There will also be a decrease in construction and renovation activities supported by the NCI.

Directives Resulting from FY 1980 Appropriations Committee Reports

An increase was provided for investigator-initiated research grants. This increase in funds will enable expansion of research in such areas as epidemiology, carcinogenesis, nutrition, clinical trials and basic research concerning the processes in malignant cells that cause tumor growth. The increase will allow NCI to maintain a steady level in the total number of grants supported.

An increase was also earmarked for the National Toxicology Program. These additional funds were provided to allow the NCI to increase the number of new chemicals that will be put on test in 1980 as well as to expand current efforts to develop and validate more rapid, inexpensive and accurate *in vivo* and *in vitro* tests of chemicals to determine cancer-causing potential. Additional positions were also provided.

An increase in funding will allow for expansion of preclinical and clinical studies on biologic response modifiers, including human interferon. The materials are preponderantly natural in origin and may increase resistance to cancer by modifying the body's biological response to tumor cells or by complementing the effect of other therapies.

Additional funds were provided to support an increase in stipends and institutional allowances for 1,555 full-time equivalent trainees.

FY 1982 Program Changes

Research on the cause and prevention of cancer will emphasize studies to understand the control of certain genes capable of causing cancer. Such genes will be isolated and identified using recombinant DNA technology. Human herpes virus genomes will be examined in light of post-transcriptional gene splicing. Other efforts will include studies on the interaction of oncogenic viruses and the immune system, and on the development of screening evaluation methods for use in large populations.

With regard to the High Energy Neutron Therapy Program, the number of clinical trials with DT generator and cyclotron facilities will increase during FY 1982. This expansion will represent exploration into disease sites not previously studied. Construction of additional cyclotron facilities will continue, with clinical trials anticipated to start during FY 1983. The Biological Response Modifiers Program will expand the numbers of materials evaluated experimentally and those available for clinical testing.

In the Large Bowel Cancer Project studies which may be ready for implementation include: the selective irradiation of tumors with slow neutrons, through the use of a neutron-capturing agent combined with tumor localizing antibodies; and chemotherapy of human adenocarcinoma, utilizing quinazoline analogs of folic acid as well as polyglutamyl derivatives, and a 10-formyl modification administered alone and in combination with 5-FU.

The Diet, Nutrition, and Cancer Program will initiate activities to study the special nutritional needs of pediatric cancer patients.

The Smoking and Health Program will initiate cross-validation studies of smoking cessation techniques, epidemiologic studies on the effects of newer low-tar, low-nicotine cigarettes, studies on the role of nicotine in smoking habituation and cessation, and studies on the joint effects of smoking with other environmental carcinogens.

The Cancer Control Program will initiate a long-term field test in screening for breast cancer to determine optimum screening periodicity, relative efficacy of low dose mammography, and the evaluation of new nonintrusive screening methods.

Summary of NCI's Research Plan Review Session with the Director, NIH

Economic constraints and heightened public accountability necessitate renewed emphasis on collective efforts to address the critical issues which affect the NIH and the larger research enterprise. Essential to this effort is the sharing of ideas and experience with those affected by the policies we pursue. The presence of members of the NCI advisory structure as well as that of Drs. Bennett, Blumenthal and Riecken, representing the Director's Advisory Committee, underscored the value of such interaction. Please extend my appreciation to Drs. Lederberg, Pitot, and Seitz for their contributions.

NCI Reorganization

A major phase of the recent reorganization--the separation of program management from grant and contract administration and from peer review--is essentially complete. The reorganization should integrate better NCI research and training activities, bring the NCI organization more nearly into conformity with that of other Institutes, and provide grant applicants in all program areas an increased opportunity to compete in the total dollar pool. Senior Institute management is now in a better position to make joint decisions concerning the allocation of funds and to tailor funding mechanisms to program needs. The reorganization has also enabled the Institute to augment its investment in research project grants vis a vis other support mechanisms. This increased emphasis on investigator-initiated research is consistent with the policy adopted by the National Cancer Advisory Board.

The final phase of the reorganization awaits Departmental approval. NCI has proposed that the existing Division of Cancer Control and Rehabilitation be abolished and a new Division of Resources, Centers, and Community Activities be established. This Division would incorporate the cancer control, centers, training and education, construction, and the organ site programs.

New Prevention Emphasis

Creation of the new Division will also allow more effort in applied prevention--an area characterized by much Congressional, Administration, and public interest. Prevention activities and projects are spread throughout the NCI, and a description of current prevention activities is being compiled by all Divisions as a preliminary step towards identifying areas for special emphasis. A major focus of the new Division will be efforts to apply what is known about prevention, while the Division of Cancer Cause and Prevention will continue its research in the etiology of cancer. For both components, the NCI investment in prevention will be determined primarily by scientific opportunities, as tempered by the total funding outlook. In FY 1979, $300 million was directed toward prevention.

Recent Special Initiatives

Four NCI initiatives address public health problems related to cancer and involve collaborative activities with other Federal agencies:

1. National Toxicology Program (NTP)

Under the new National Toxicology Program (NTP), the NCI continues its program of animal testing for carcinogenicity of suspected environmental chemicals. The NTP addresses the major research and regulatory needs in toxicology testing. The Program involves the relevant activities of the NCI and three other agencies, the National Institute of Environmental Health Sciences, the Food and Drug Administration, and the Center for Disease Control--National Institute for Occupational Safety and Health. Although NCI provides the major share (70%) of the cost and program resources, these agencies work under a centralized organization to evaluate the toxicity, including carcinogenicity, of environmental agents.

In FY 1979, 79 chemicals were started on test. This number should increase to 100 per year in the future if funds permit. Because all environmental chemicals cannot be tested in long-term animal experiments, efforts are in progress to develop rapid, inexpensive laboratory tests of chemicals for cancer-causing potential.

2. Low-Level Ionizing Radiation Research

The possible cancer-causing effect of exposure to low-level ionizing radiation, such as that resulting from diagnostic radiation or occupational exposure, has recently received increased attention.

In response to these concerns, a variety of Federal efforts were undertaken. One comprehensive study reported by the Interagency Task Force on the Health Effects of Ionizing Radiation was commissioned by the White House in May 1978. The resulting report emphasized the potential dangers of radiation exposure and made recommendations for a coordinated Federal program on the health effects of ionizing radiation, particularly nuclear-related projects. The report concluded that, in general, the risks of low-level radiation are very small, but potentially greater than has been stated before.

At the request of the White House and the Congress, the Committee On Federal Research Into The Biological Effects Of Ionizing Radiation was created. The Committee was charged with:

- Establishing a comprehensive program of research into the biological effects of low-level ionizing radiation.
- Conducting a comprehensive review of Federal programs of research on the biological effects of ionizing radiation.
- Consulting closely with all concerned agencies in the conduct of planning and design studies for epidemiological research on the health effects of low-level ionizing radiation.

Aspects of these responsibilities were delegated to the National Cancer Institute, where a Radiation Research Group has been established. In addition to providing staff support to the interagency committee and to the Directors of NIH and NCI in radiation matters, the NCI Group is responsible for developing a long-range program for NIH research in low-level ionizing radiation.

3. Saccharin

Experimental evidence confirming that saccharin causes bladder cancer in rats and mice suggested that the compound is a potential human carcinogen. The Food and Drug Administration proposed a ban on the use of saccharin as a food additive in such products as diet sodas. Saccharin would still be permitted for use in tabletop sweeteners, with appropriate warning labels. Because of strong public opposition to this, the Congress imposed an 18-month moratorium on the proposed ban.

A 1978 National Academy of Sciences report on the saccharin study concluded that:

- In rats, saccharin is a carcinogen of low potency.
- Saccharin promotes the cancer-causing effects of some other carcinogenic compounds in rats.

The NCI and FDA collaborated in a large-scale population-based study of saccharin in relation to the development of bladder cancer. Data collected from about 3,000 new patients with bladder cancer and about 6,000 controls confirmed the animal findings and established the fact that saccharin must be viewed as a carcinogen in humans.

4. Asbestos

Much attention has been given by the NCI to informing Americans about asbestos, a fibrous heat-resistant material which has been linked to a high rate of lung cancer and other serious diseases among workers in the shipbuilding and construction industries. Because so many people have been exposed to this carcinogen, the NCI organized, on behalf of HHS, an Asbestos Awareness Program on the possible hazards of such exposure. Communication techniques for mass dissemination of information included printed and audiovisual materials. Educational materials were also developed for health professionals describing the nature of the health risks from asbestos and outlining steps physicians might take when diagnosing or treating patients.

Civil Rights and Affirmative Action Initiatives

I appreciated the report on the Institute's Equal Employment Opportunity program and the opportunity to learn more about current activities and future plans in two EEO special emphasis areas--the Federal Women's and Hispanic Employment programs:

- Significant progress has been made during the past year in implementing the Affirmative Action Plan and in pursuing priority action items identified by the NCI EEO Advisory Group.

- In the coming year, emphasis will be placed on strengthening the role of the External EEO Public Advisory Committee and on efforts to increase the number of women and minorities in the Summer Employment Program, Clinical Associates Program, and managerial and policy positions.

- The NCI participates in both the Minority Access to Research Career Program and the Minority Biomedical Support Program. The annual NCI support of these two programs is $2 million.

- Efforts to further develop the Federal Women's and Hispanic Employment Programs have been directed toward recruitment, career counseling, and community outreach activities.

Consensus Development

NCI consensus development conferences planned for 1980 will examine adjuvant therapy in breast cancer, immunodiagnosis, and cervical cancer screening. A consensus development meeting will also be held on computerized tomography of the central nervous system sponsored jointly with NINCDS and the National Center for Health Care Technology.

Division Emphases

- Division of Cancer Biology and Diagnosis. A new research tool--hybridoma methodology--holds promise for the early detection and possible treatment of cancer. This new technique enables investigators to produce large quantities of pure antibodies and has led to the demonstration of a specific surface molecule on a human tumor, not present on normal cells, from mice immunized with human melanomas. Additional cancer studies are in progress using hybridomas secreting monoclonal antibodies to various human cell surface antigens. The technique is in the developmental stage, and its potential application to research in diverse areas is under active exploration.

- Division of Cancer Treatment:

  1. Biological Response Modifiers program--Many such substances are made by the body and in some way alter its response to cancer. Because of their nature and their action on the host rather than the tumor, they may be less toxic than chemotherapy. This year the NCI will purchase interferon to initiate studies to evalute whether the positive clinical findings that have been reported for a few patients can be confirmed. Another biological response modifier is the vitamin A analog, 13-cis-retinoic acid. Animal studies indicate that this agent prevents cells from becoming cancerous. Plans are to have available a cadre of clinical investigators ready to initiate new clinical studies on short notice.

2. Neutron Therapy--Three contracts have been awarded for construction of neutron generators and for clinical trials on 3,000 cancer patients to evaluate this promising new high energy form of radiotherapy. Neutrons have an advantage over conventional X-rays because their effect is less dependent on oxygen, thus offering a possibility of activity against large tumors that have oxygen-deficient regions.

- Division of Cancer Cause and Prevention:

1. Intramural program--Based upon site visits by the DCCP Board of Scientific Counselors, this program is being restructured to strengthen epidemiological research and to link it to laboratory research and to enhance research relevant to occupational cancer and other exposure to carcinogens.

2. Occupational factors--Occupational factors are increasingly important, accounting for more than 50,000 new cases of cancer a year. The Institute has expanded its research efforts to include testing of occupationally-related chemicals and agents for carcinogenicity and epidemiological studies on workplace exposures to carcinogenic agents. These efforts include 68 collaborative projects developed with NIOSH since 1976.

- Cancer Control and Rehabilitation:

1. Smoking, Cancer and Health Program--Program emphasis will shift from development of a less hazardous cigarette to the development of grant programs in smoking prevention and cessation and epidemiologic studies to assess low tar and nicotine cigarettes.

2. Diet and Cancer--Some animal and epidemiological studies suggest an association between diet and cancer. Pressure to advise the public of a diet that can minimize cancer risk continues. Interim principles that were issued are now being reviewed, and the National Academy of Sciences will conduct a three-year assessment to develop dietary guidelines.

3. Cancer centers--There are currently 21 comprehensive centers and 41 specialized centers. They have developed into an important national resource, and depend heavily upon NCI support for stability.

Stabilization of the Science Base

Although the NCI agrees generally with the desirability of stabilizing the science base, and that research project grants should receive the highest priority in any plan, the NCI does not agree that fixing an absolute number is the most effective approach for accomplishing stabilization. The establishment of a fixed number greatly decreases an Institute's flexibility in the management of its budget and in responding to evolving needs and opportunities.

Chapter 6

NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

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Chapter 6

NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

Director's Preface

During and immediately after pregnancy, the developing person is most vulnerable to adverse change. The consequences of physical and psychological damage early in life may not be apparent until adulthood. Illustrative of the immediate consequences of early insult are these data on health problems that fall within the province of the National Institute of Child Health and Human Development (NICHD):

- In 1977 in the United States, fourteen infants died for every 1,000 born alive. The death rate for black infants was 24 per 1,000 live births.

- Of all infant deaths, two-thirds occur in those weighing less than 5.5 pounds (2500 grams). Infants who weigh less than 2500 grams are 20 times more likely to die within the first year of life. Of those who survive, twenty-five percent will be handicapped for life.

- Congenital malformations are the second leading cause of death for children one to four years; one-sixth of all infant death is caused by birth defects.

- The leading cause of death for infants after the age of one month continues to be the Sudden Infant Death Syndrome which yearly claims two of every 1,000 infants born alive.

- In 1977, 570,609 births occurred to adolescents 19 years old and younger. Expectant mothers less than age 15 are at higher risk of complications of pregnancy and birth than older adolescents; 70 percent of those less than age 15 receive no care during the first months of pregnancy.

- In 1977, there were 249,800 out-of-wedlock births to women under the age of 20; 10,000 to women under age 15 and 120,800 to women aged 15 to 17.

- Teen-agers continue to account for almost one-third of the total number of legal abortions. In 1976, women under the age of 20 received 370,000 abortions, over 15,000 of them to women under the age of 15.

- Reading and learning disorders affect as many as twenty percent of all school-age children.

- An estimated six million Americans suffer from mild to severe mental retardation. Each year, approximately 100,000 children are diagnosed as mentally retarded; each decade therefore adds 1,000,000 people to the cumulative number of the retarded population.

Long-range consequences of early disease and disorder are less quantifiable but we know, for instance, that obesity is a contributing factor to hypertension and diabetes; that poor nutrition may affect the development of adequate immune systems and may compromise reproductive health; and that early and unplanned childbearing places both the mother and her infant at prolonged educational and economic disadvantage. Increasingly too, evidence mounts that life styles and habits ingrained in childhood can impact upon adult well-being. For example, the concern to prevent children from smoking is testimony to the cardiovascular problems and risks for cancer that may ensue. The NICHD is charged with responsibility to relate research to the breadth of health and behavioral problems represented above.

Research Strategy

The NICHD fosters and supports a multidisciplinary program of research in reproductive biology, demography and epidemiology, developmental biology and perinatology, and the social and behavioral sciences. These disciplines are arrayed across ten research program areas including: Pregnancy, Birth, and the Infant; Sudden Infant Death Syndrome; Congenital Defects; Nutrition; Child and Adolescent Development; Mental Retardation; Fertility-Infertility; Contraceptive Development; Contraceptive Evaluation; and Population Dynamics.

The ten research program areas have important relationships one to another. For example, a significant number of premature and low birth weight infants can be attributed to unwanted pregnancies, particularly among adolescents. Evidence indicates also that early childbearing places both the mother and her infant at increased risk for physiological and psychological problems with long-term implications. Solutions, therefore, to questions on the acceptability of various methods of contraception and their safety will have direct impact upon the health and well-being of mothers and infants. Studies in nutrition can have relevance both for pregnancy outcome and the management of distressed newborns as well as to the regulation of fertility and to reproductive health. Moreover, nutritional problems may have impact on behavioral outcomes.

Research Goal

The essential goal of the NICHD is to implement the major national effort of multidisciplinary research to provide all couples with safe, effective and inexpensive means to regulate fertility and assure that all infants from conception and birth are provided opportunity for a healthful and productive adulthood.

The Institute's Research Plan reflects its continued commitment to this goal and details areas that will be continued and strengthened in order to preserve and maintain this valuable science base.

FY 1981 Program Changes

Major Activities to be Initiated in FY 1981

No new programs will be initiated in FY 1981.

Major Activities to be Maintained in FY 1981

The FY 1981 budget increase is limited to research project grants only. The Institute will protect research efforts on critical problems of reproduction, pregnancy, infancy, and childhood.

- Reproduction--A science base in reproductive biology will be maintained. Areas of emphasis continue to include contraception (both male and female), human fertility, fertilization and implantation, and nutrition and reproduction.

- Pregnancy and Infancy--Efforts will continue to elucidate mechanisms responsible for poor pregnancy outcome. Specific attention will be given to maternal-fetal interactions and the changes produced by maternal diseases such as diabetes, toxemia, and infection.

  -- Research in genetics and teratology will be maintained. Investigations in human embryology will be supported with emphasis on chromosomal changes and aberrant immunological mechanisms that contribute to congenital defects.

  -- Continued emphasis will be given to the prevention of mental retardation and to the program of genetic research on trisomy 21 (Down's syndrome).

- Childhood--Programs will be maintained in learning, reading, and cognition; parent-child relationships, including early mother-infant bonding; the impact of socio-environmental factors, particularly the family, on the development of children born at biological risk; and on the prevention in children of smoking and other behaviors harmful to health.

Major Activities to be Cut Back, Eliminated, or Not Started in FY 1981

Because the FY 1981 increase is limited to research project grants only, the following major contract research activities will be affected:

- A program on special problems of adolescent contraception will be curtailed.

- A major contract program on the evaluation of brain function associated with information processing in reading disabled children will be reduced.

- Initial clinical evaluation of a method to predict ovulation for use in natural family planning will be delayed.

- A study to focus on cardiovascular risks for vasectiomized males will be postponed.

- Ongoing research on migration and distribution consequences of fertility, and population trends will be hampered in growth.

New centers and program project awards planned for initiation in FY 1981 will be delayed in fertility and implantation, male reproduction, adolescent fertility, and population migration and distribution.

Impact of 1980 Congressional Appropriations Reports on FY 1981 Plans

The FY 1981 plans for the NICHD will attempt to be responsive to Congressional interest in research on pregnancy and birth, nutrition, and the reproductive sciences. The Congress encouraged the Institute to expand studies on Down's syndrome and on the interrelationships of diabetes and pregnancy. Continued support of behavioral and social science research in the area of adolescent pregnancy reflects Congressional concern for Institute leadership on this health problem.

FY 1982 Program Changes

- Pregnancy, Birth and the Infant--The program has emphasized development of new knowledge on the effects of acute hypoxia on fetal development with particular attention to investigations on changes observed in uterine, placental, and fetal circulatory patterns following maternal exercise, stress or smoking. In FY 1982, emphasis will be placed on the more subtle effects on fetal development of chronic oxygen deprivation. Patterns of fetal breathing will be studied as will mechanisms by which the fetus adapts to a less than optimal intrauterine environment. In an effort to identify and clarify mechanisms that contribute to stability in pregnancy within the maternal-placental-fetal unit, studies will be supported on the morphology, physiology, metabolism, and aging of placentas for normal and high risk pregnancies. As a part of the continuing effort towards preventing prematurity and the birth of low-birth-weight infants, activities are planned to elucidate the maternal and fetal roles in the onset of human labor. Studies will also be encouraged to add to the existing knowledge on neonatal disorders that may compromise successful adaptation to extrauterine life.

- Sudden Infant Death Syndrome (SIDS)--Efforts will be directed towards strengthening the science base of research to categorize infants who are at risk of SIDS. Much of the science base is expected to be provided by data obtained from the Cooperative Epidemiologic Study of SIDS Risk Factors. Exploratory multivariate analysis of the first 200 cases and 400 matching controls will have been completed early in FY 1981. Using the results of the exploratory analyses on this first sub-sample of the data, hypotheses formulated by the study's Steering Committee and consultants will be tested on the total data set of 850 cases and 1700 matching controls. The results of this hypothesis testing will be available early in FY 1982. These results, with refinements as needed, will provide the base for a structured oral presentation of findings to the research and clinical communities during the second quarter of FY 1982. Written publication of results is expected to occur by the end of FY 1982 or early in FY 1983. Subsequent to the publication of study results, data tapes will be available to investigators interested in specific aspects of post-neonatal infant development, including SIDS.

- Congenital Defects--More emphasis will be directed to studies of genetic, cultural, and environmental factors that regulate or interfere with normal development. Special efforts will be devoted to genetic disease associated with gross structural abnormalities in an attempt to identify the specific genes and mechanisms that contribute dually to both types of defect. Maternal, paternal, and fetal exposure to potential teratogenic drugs and agents will be evaluated as causes of newborn congenital malformations. The "half-sibling" model using the offspring of pairs of human twins will be employed in an effort to separate out environmental from genetic factors responsible for normal and abnormal developmental patterns. Developmental defects in infants of diabetic mothers will be studied to evaluate maternal as well as genetic factors in multifactorial disease. Abnormal patterns will also be studied through the development of animal models. Clinical and epidemiologic studies are to be emphasized, along with basic biological research, to focus on developmental defects in children.

- Nutrition--Studies are planned on the complex problem of determining the nutritional status and functional nutrient requirements of the pregnant woman and her fetus. Because the theoretical basis for nutritional management of low-birth-weight infants is not well understood, an important research priority continues to be the determination of daily nutrient requirements and tolerances of infants who are premature or small for gestational age. New analyses will be encouraged on the behavioral, social and cultural factors that determine appetites, food preferences, eating habits and nutritional status of infants, children, adolescents, and pregnant women. New research is planned on the precursors and determinants of infantile and childhood obesity. More behavioral and social science research is planned on the problems of differential weight gain during pregnancy and on growth retardation during infancy and childhood. Immunological factors of breast milk will be further analyzed to determine antimicrobial components that work to prevent neonatal infections. A new interdisciplinary program will involve the search within the central nervous system for mechanisms that control taste preferences, eating and drinking behavior, gastrointestinal function, fat storage, and body composition.

- Child and Adolescent Development--Following upon a major Institute-sponsored conference on female maturation, a program of research will be initiated on the psychological, psychobiological, and social development of women, from infancy to maturity. Studies on healthy social development will be expanded from the earliest manifestations of mother-infant bonding to the development of competence and assumption of adult roles. Emphasis will be placed on the identification of specific impediments to healthy social development at various developmental stages. Studies on adolescent development are planned to further understandings on the complex series of events that lead from dependent childhood to autonomous adulthood. Continued attention will be given to studies on the complex interrelationship of communicative and intellectual competencies as they develop from infancy to adulthood, and to the psychological, social, and environmental influences that foster or impede their healthy development.

- Mental Retardation--Research on genetic problems related to mental retardation will be continued with expanded effort given to studies to determine the extent of paternal contribution to Down's syndrome and whether paternal age affects its incidence as does maternal age. New resarch will be directed toward elucidation of the full clinical picture of the recently discovered "fragile X" syndrome which is the most frequent cause of mental retardation of genetic origin in males. Research activity on prevention of mental retardation in children from psychosocially disadvantaged homes will be continued with emphasis upon child-focused strategies and other models for intervention aimed at producing sustained intellectual gains. Studies are needed with special emphasis on biologically impaired children to determine the processes and mechanisms within the family environment that can become effective agents for teaching and socialization. The extensive use and misuse of pharmaceutical drugs, chemical agents, and alcohol during pregnancy are known to have teratogenic effects on offspring. Exposure in less severe form may also result in intellectual and behavioral impairment without evidence of morphological change, as in cases of low lead levels. Expanded study is needed to identify teratogenic influences that can be related to depressed mental performance and disordered behavior.

- Fertility-Infertility--Efforts to expand the science base in reproductive biology and medicine will continue. Among the areas of emphasis are brain regulation of reproductive hormones, the mechanism of action of reproductive hormones, and physiological and biochemical aspects of male and female reproductive functions and processes. If confirmed, recent reports of declining sperm counts in American men could have important implication for human fertility. Research on male reproduction will therefore be emphasized through additional studies on the mechanisms of immunological interference with normal reproductive function. New initiatives are planned on fertilization, implantation and early embryonic development in mammals, and on the underlying causes of human infertility. A new initiative is planned on reproductive disorders. In women, such disorders as endometriosis, dysmenorrhea, and polycystic ovarian syndrome will be investigated. In men, studies will be aimed at the alleviation or cure of such disorders as prostatitis, prostatic hypertrophy, and varicocele. Studies on human infertility in the male will be concerned with congenital and secondary occlusions of the male reproductive tract, environmental effects on sperm production, the importance of genetic factors in abnormal sperm production, and psychological factors affecting sexual activity and semen quality. Research on infertility problems in the female will involve studies of the cervix, the uterine environment, and tubal factors such as anatomical defects and infection. Infertility research on couple factors will include immunological studies, marital and coital problems, and studies of the psychological effects of the processes leading to and involved in diagnosis and treatment.

- Contraceptive Development--Research will be expanded and initiated in areas that provide maximum opportunity to build understandings on a variety of approaches to contraception. Contraceptive efficacy trials are planned, for example, to demonstrate the utility of synthetic neuroendocrine hormone (LHRH) as an inhibitor of ovulation, a postcoital

antifertility or luteolytic agent, and male contraceptive. The long-term safety of these drugs will be an important emphasis. Clinical trials are planned on natural estrogens and new oral formulations. Evaluation activities will be supported on implantable and injectable biodegradable drug delivery systems, on new long-acting progestins (injectable drugs), and on new spermicidal barrier methods. Promising new compounds directed at finding safer drugs to regulate fertility will be investigated.

The search for luteolytic agents and potentially useful antiprogestins will be continued. Luteolytic agents interfere with the secretion of progesterone (the female hormone required by the uterus for the development of the fertilized egg) and thus can make the female infertile. Chemical and biological efforts have endeavored to find a luteolytic agent among chemical entities, other than LHRH analogs, such as prostaglandins and steroids. Primate testing will be expanded to determine the potential of those currently available prostaglandins and steroids. Primate testing will be expanded to determine the potential of those currently available prostaglandins and steroids as luteolytic agents. New chemical entities will also be tested.

- Contraceptive Evaluation--Research in contraceptive evaluation will include studies of the safety and efficacy of methods currently in use. Such studies may involve newly developed methods now at the preclinical state but emphasis will be placed on older methods of contraception. Additional studies will focus on the relationship between contraception and neoplasia, specifically breast and cervical cancer, and between lactation and the use of contraceptive steroids. Investigations of the sequelae of female sterilization will be expanded as will studies on the reversibility of male and female sterilization. Based on epidemiologic leads, efforts to determine mechanisms of the side effects of contraceptive steroids will be developed. A program investigating the safety and efficacy of contraceptive methods used by teenagers will be expanded. Studies will focus on the interactions between venereal disease and contraception, the risk of cervical dysplasia among young women, and the determination of safe contraceptives for use by young women with severe medical problems. It is anticipated that in this fiscal year, basic metabolic studies on the effects of hormonal contraceptives can be sharply reduced as can studies on the relationship between contraceptive use and later involuntary infertility. Research will be initiated to evaluate the effects of different oral contraceptive formulations currently in use on serum lipoproteins in women. Studies in nonhuman primates will also be developed to assess the effects of various individual estrogens and progestins on serum lipoproteins, and to relate these effects to the rate at which atherosclerosis develops. In addition, research will be initiated to test the hypothesis that one or more of the synthetic steroids used in oral contraceptives may stimulate formation of specific antibodies, and that these antibodies may be involved in the etiology of thromboembolic disorders or other health effects that occur among some women using the pill.

- Population Dynamics--A major initiative is planned on women's roles and fertility to improve understandings of both the determinants and consequences of fertility behavior on an individual and couple basis. Additional research is planned on the family structure, marital stability, and the changing roles of women. Emphasis will be placed on the effects of timing and spacing of births and family size on the well-being of children, especially those born of adolescent mothers. The consequences of family instability on the welfare of children will receive careful attention. A major emphasis of research will involve the factors influencing choice of the contraceptive and effectiveness of its use as a means to address the still high incidence of unintended pregnancies, a tendency to delay childbearing and hence to require contraceptive protection rather than sterilization, and the unlikelihood of the development of a new contraceptive within the next five. years. Research on adolescent fertility will include studies on trends in behavior for this age group and will also emphasize the antecedents of early sexual and fertility-related behavior. Efforts undertaken concerning the practice of contraception will have particular relevance for this age group. Of special interest regarding the consequences of early childbearing are the relationship of child mortality to the age of the mother, and the effect of early childbearing on the parental family.

Summary of NICHD's Research Plan Review Session with the Director, NIH

Program Overview

The NICHD conducts and supports research that focuses on the continuum of human development--from infancy and childhood, through adolescence and adulthood. The Institute has two major extramural research programs, the Center for Population Research (CPR) and the Center for Research for Mothers and Children (CRMC), and an Intramural Research Program.

- CPR--This program supports and conducts research on reproductive biology and endocrinology, fertility-infertility, social and behavioral aspects of reproduction and population change, and contraceptive development and evaluation. Approximately 40% of the Institute's budget is invested in this area, which features a large contracts program.

- CRMC--This program supports and conducts research on pregnancy and infancy, SIDS, developmental biology and nutrition, mental retardation, and child and adolescent development.

The cost-benefits attributed to this Institute are vast because much of its research has application for disease prevention. Two areas of study where this becomes evident are diabetes and mental retardation research. NICHD supported studies on high-risk pregnancy to enable diabetic mothers to have normal pregnancies and prevent conditions that require long term care and treatment. Mental retardation research has the potential to prevent conditions that impair the quality of life and impart life long disability. The cost-benefits realized from research advances in these two areas alone are substantial.

The NICHD expresses its research program in 10 areas of major importance. The emphasis areas were initially developed for planning purposes in concert with your National Advisory Council. They are now utilized for budget purposes as well, and represent the most important areas of scientific focus for the Institute. Allocation of resources among these 10 areas is based primarily on scientific opportunity and, to some degree, historical funding trends. The Advisory Council Planning Subcommittee also provides advice in the allocation of resources.

Stabilization of the Science Base

A major portion of the discussion focused on the proposal to stabilize NIH support of the science base, particularly as it would apply to predictable funding for research project grants.

Stabilization would affect NICHD disproportionately because a number of important research programs are supported by the contract mechanism; contracts support 15% of extramural research. Therefore, in order to stabilize research project grants within a constrained budget, funds would be taken from other catagories of support. This action would result in no new training awards and no new awards for research in contraceptive development and contraceptive evaluation which is supported entirely through the contract mechanism. Center

awards would be reduced by more than one-half the present number and special areas of research emphasis would be eliminated. In FY 1982, the Institute would maintain an adequate level of support for training, and develop its social and behavioral research programs before stabilizing the level of competing research projects.

Population Program Authorization

Although most of NIH's research programs are authorized under Section 301 and Title IV of the Public Health Service Act, the population research program of NICHD is authorized under Title X. This has created some problems for the Institute because:

- the program under Title X is restricted by time and dollar limits for administration, as well as program, and must be reauthorized every three years, unlike most research programs authorized under Title IV and Section 301, and

- to implement Title X, a position, the Deputy Assistant Secretary for Population Affairs (DASPA), was statutorily created with line authority to control all population activities, including research.

Training

NICHD anticipates difficulty in maintaining an adequate number of trainees in the future. Training is supported in the medical specialties of obstetrics and gynecology, in developmental biology, and in the behavioral sciences. The NICHD has a significant behavioral science research training program. Research training in the behavioral sciences, unlike that for the biomedical sciences, is primarily predoctoral. Therefore, the Institute feels that it is essential to maintain an adequate base of predoctoral training in the behavioral sciences. Behavioral sciences research training at the NICHD provides the major focus of training for developmental psychology in the Department.

Nutrition

- A conference on Nutrition, Behavior, and the Life Cycle, cosponsored with NIA in June, 1979 was quite successful.

- Four of the Institute's Major Research Programs (P50 centers) are heavily involved in nutrition research. The Institute has chosen to augment the support of clinical nutrition research through supplemental funding in these existing centers.

- The Institute has stimulated the field of behavior and nutrition research through the publication of RFP's and program announcements. The Institute has funded five new contracts on nutritional individuality and anticipates receiving many new grant applications on the behavioral aspects of nutrition (e.g., development of taste, food preferences and aversions, eating habits and lifestyles).

Fertility/Infertility

Two contracts to fund clinical trials on luteinizing hormone releasing hormone (LHRH) have been awarded to test the effect of peptide analogs of this hormone on fertility regulation in males and females. The results of these clinical studies have important implications as these peptide analogs would represent a new class of compounds for contraceptive use.

Major Civil Rights and Affirmative Action Initiatives

During FY 1979 the Institute's EEO program has provided training for managers and the EEO Committee, emphasized women's needs, and worked toward the development of a conference to encourage minority institution support and Hispanic participation in the MBS program. Plans in 1980 call for increased participation by minorities and women in grants and contracts, and the development of EEO performance objectives for SES (Senior Executive Service) personnel and merit pay supervisors (grades GS-13 to GS-15).

Clinical Research Facility

The feasibility study you provided Congress at their request contained four recommendations:

"-- A Federal Pregnancy and Infancy Study Center should be established for investigation of maternal and newborn health problems.

-- The center should be located within a host institution already distinguished for quality of research and obstetric and perinatal care. The space for the center should be leased from the institu- tion.

-- A study should begin immediately to define the characteristics desired of a host institution for the center, to establish resource requirements, and to plan a development schedule.

-- The NICHD should complete the formation of a perinatal research network by awarding additional major research programs for coordination by the Pregnancy and Infancy Study Center."

We discussed the continuing need for such a research center to focus on perinatal biology and reasons for why this should be an intramural, off-campus program rather than an extramural one. USDA nutrition centers were cited as a model of the type of university located, intramural Federal laboratory that is envisioned. In view of NIH interest in stabilizing the research environment, further consideration should be given to how this departure from usual support patterns would affect outside institutions.

Drs. Childs, Lash, Hetherington, and Pritchard, members of the National Advisory Child Health and Human Development Council, participated in the review session. Their perspectives were a valuable contribution to the discussion.

Chapter 7

NATIONAL INSTITUTE OF DENTAL RESEARCH

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Chapter 7

NATIONAL INSTITUTE OF DENTAL RESEARCH

Director's Preface

The National Institute of Dental Research (NIDR) is responsible for facilitating the development of new knowledge concerning the cause, prevention, diagnosis and treatment of oral health problems. The Institute focuses on the support and conduct of investigations related to dental caries, periodontal diseases, craniofacial anomalies, soft tissue diseases and problems, nutritional factors associated with oral health, restorative treatment materials, pain mechanisms and control measures, as well as behavioral and social studies of oral health and its promotion.

Significance of Oral Health Problems

It has been estimated that two-thirds of the population in the U.S. are currently in need of some kind of dental treatment (NCHS:HANES 1971-1973). The result of neglected treatment commonly is pain, loss of teeth and destruction of the supporting structures of the teeth which can lead to disfigurement, impaired speech and chewing ability, as well as difficulties in social interactions.

In 1971, almost 15 percent of the American public was edentulous, including 45.5 percent of those 65 and over. Dental caries is the most common oral disease in the United States and is the primary cause of tooth loss through young adulthood: by age 35, the average American has lost five teeth and 11 more have been attacked by this disease. Periodontal diseases affect nearly 75 percent of the adult population in this country and are the most common cause of tooth loss in people over 35 years of age, being responsible for 80 percent of extractions in persons over the age of 45.

Nearly 6000 babies are born each year with some form of cleft lip or palate, or both, continually adding to the total of nearly 300,000 persons affected by these conditions in the U.S. Such conditions make up 13 percent of all birth anomalies, second only to clubfoot as the most common birth defect. Over one-half of all children are estimated to have malocclusion. A large segment of our population (at any given time about 20% of the population, 70% of whom endure recurrent discomfort) experiences oral ulcerative disturbances and over 7000 American lives each year are lost because of oral cancer.

The nation's dental bill of ten billion dollars in 1977, 5.6 million days lost from work in 1976, 4.4 days/100 persons with bedridden disability attributable to dental conditons in 1975, reflect the enormous economic and social burden that these oral health problems precipitate.

Research Goals and Strategies

Of the wide range of oral diseases and related abnormalities experienced by Americans, the two most prevalent problems are caries and periodontal diseases, and thus these two program areas receive high priority in this Institute. With respect to dental caries, the major emphasis is placed on research on preventive measures since to a large extent, this disease is irreversible. In a targeted effort to improve existing caries prevention technology and to develop new methods, the National Caries Program conducts research directly and supports extramural research in four strategy areas: combating the microbial agent; enhancing tooth resistance; improving diet and nutrition; and improving delivery mechanisms. Considerable insights have been gained particularly in the second area and any new resources would be focused on an effort to move from clinical trials to field evaluation of techniques and technology transfer.

With respect to periodontal diseases, less is known about their etiology than is known about the etiology of dental caries. For this reason, research has focused on the role of infectious and immune processes. Recent strategies have permitted studies of agents to control oral microflora and mechanisms to motivate people to remove dental plaque for themselves. To expedite studies in the human, the NIDR has funded three specialized clinical research centers in this field.

Emphasis in the craniofacial anomalies area is on the expansion of knowledge related to early embryonic craniofacial development, biochemical and molecular alterations leading to oral-facial clefts and on treatment modalities--until the time when the knowledge base permits development of prevention technology.

Continued support will be given to research on etiologic and epidemiologic factors associated with oral ulcerative disease, oral cancer, disturbances of mineral metabolism, and nutritional factors in oral health. To repair damaged tissue and to preserve the integrity of the oral cavity, the development of improved dental materials and restorative procedures must continue. Because pain is symptomatic of many oral-facial conditions and can be associated, together with fear and anxiety, with dental treatment, the Institute plans to continue its support of studies examining the cause and mechanisms of oral pain, as well as its prevention and therapy. Associated with the above strategies is a need for behavioral and social research which focuses on aspects of epidemiology, prevention, diagnosis and treatment for each of the oral diseases and conditions. This latter area constitutes an increasingly important new activity for the NIDR.

FY 1981 Program Changes

Major Activities to be Initiated in FY 1981

None

Major Activities to be Maintained or Expanded in FY 1981

Caries

- Transfer of information concerning community-based self-applied fluoride programs;
- Studies related to the potential development of a caries vaccine;
- Research on non-cariogenic sweeteners;
- Development of intra-oral devices for slow-release of caries preventive agents;
- Clinical research on new highly effective fluoride-based agents; and
- Fundamental research on population and colonization of bacteria on oral surfaces.

Periodontal Diseases

- Research on etiology, microbiology and immunology of periodontal diseases such as studies of the role of bacterial and immuno-regulatory factors in periodontal pathology;
- Ongoing studies of the relationship between periodontal diseases, systemic diseases, dietary deficiencies and immune deficiencies; and
- Support of three established specialized clinical research centers.

Craniofacial Anomalies

- Basic studies of neural crest cells and early embryonic craniofacial development;
- Research on the biochemical and molecular alterations leading to oral-facial defects; and
- Use of computerized methods to analyze structural changes resulting from various forms of treatment.

Soft Tissue Stomatology and Nutrition

- Research on metabolism of fluoride, other trace elements and minerals;
- Nutritional studies related to oral health;
- Studies on oral ulcerative diseases and oral cancer; and
- Basic studies of bone biology.

Restorative Materials

- Continue development of new and improved dental materials;
- Maintain current level of effort for clinical trials of artificial tooth implants; and
- Continue development of computer-controlled feedback scanning x-ray system to assess progress of dental treatment in longitudinal studies.

Pain Control and Behavioral Studies

- Studies focusing on social and behavioral factors associated with epidemiology, prevention, diagnosis and treatment of each of the oral diseases and conditions;
- Multidisciplinary studies of pain and pain control mechanisms; and
- Research on oral motor behaviors.

Dental Research Institutes and Centers

- Basic science research will be maintained, as well as the modest increments in clinical research which were initiated in FY 1980.

Major Initiatives to be Cut Back, Eliminated, or Not Started in FY 1981

Caries

- Preclinical and clinical screening of anti-plaque and anti-bacterial agents will be curtailed.

Periodontal Diseases

- Investigations to develop pharmacologic agents for prevention and treatment will be curtailed;
- Establishment of a new specialized clinical research center will not be possible;
- Research on the development of diagnostic instrumentation will be delayed; and
- Studies to develop a controlled-release system for an antimicrobial agent will be delayed.

Craniofacial Anomalies

- Long-term studies of acquired craniofacial defects to determine incidence, prevalence and severity, and to determine factors associated with effective early care and long-term rehabilitation, will be delayed.

Soft Tissue Stomatology and Nutrition

- Ongoing intramural clinical research efforts on soft tissue diseases will be curtailed; and
- Clinical research aspects of mineral metabolism in various disorders will be delayed.

Restorative Materials

- Expansion of clinical trials of tooth implants for a prospective study will not be possible; and
- Clinical evaluation of new materials for maxillofacial prostheses will not be possible.

Pain Control and Behavioral Studies

- Expansion of multidisciplinary research program into the area of chronic pain will not be possible.

Dental Research Institutes and Centers

- Expansion of clinical research will not be possible; and
- Selected basic research projects will have to be curtailed and/or phased out.

Intramural

- Selected basic research projects will have to be cut back.

Directives Resulting from FY 1980 Appropriations Committee Reports

Senate

- Brittle Bone Disease

  In response to the comments that NIDR has not given sufficient attention to this area of research, the Institute does support studies of osteogenesis imperfecta as well as basic studies of the origin and fate of bone cells, mineral metabolism and of the influence on bone of mechanical factors, electricity, hormones and drugs. Addditional support for research on this disease would require curtailment in other areas, given current budgetary constraints.

- Training

  The Institute intends to invest any incremental training resources, as directed by the Committee, into understaffed fields such as the multidisciplinary areas of epidemiology, cariology, socio-dental sciences, and clinical trials.

- Dental Research Centers

Though the Dental Research Institutes are important as centers of excellence, as recognized by the Committee, they have had few funding increases in recent years. The FY 1980 budget permitted an increase of $500,000 which provided for replacement of some worn-out equipment. To meet their needs for continued and long-term growth, the NIDR would require considerable increments in new funds or severe curtailment of other NIDR program activity.

- Tooth Decay

As suggested, the Institute continues to expand its educational activities not only to professionals but to lay populations as well. NIDR completed and distributed to over 700 TV stations a 30-second TV public service announcement on the wise choice of snack foods. Thus far 35% of the stations have responded and indicate that "It's a Snap to Keep Your Teeth Healthy" was well received and frequently shown in time slots during children's viewing hours. Two more "spots" are now in preparation and will be pre-tested for groups of 7-9 year olds before release. Radio "spots" targeted for 10-16 year olds featuring music stars popular with children will be completed during the year and mailed to U.S. radio stations. Leaflets, posters, and stickers for youngsters will be promoted as well. New and up-dated leaflets on tooth care for pregnant women, dental sealants and fluoride were printed during the year. A new exhibit on self-applied fluoride tablets and school-based fluoride mouthrinsing programs were developed. Planned projects for the coming year include a film for the scientific community on cariogenicity and sugar, a film which will outline the National Caries Program efforts to clarify the relationship between sugar and caries. A simpler film on the same subject will be prepared for civic groups, schools and other organizations.

- Pain Control

NIDR continues to expend resources as acknowledged and approved by the Committee, to maintain research on pain. Within the amount provided, the Institute supports and conducts research on behavioral interventions related to fear and anxiety, dental anesthesia and sedation, temporomandibular joint pain, and basic studies of pain mechanisms.

- Diabetes

In FY 1981 the Institute will maintain studies related to the viral etiology of diabetes mellitus, as suggested by the Committee. It will also maintain its effort focused specifically on the relationship between diabetes and periodontal diseases which was initiated during FY 1980 as a result of a modest expansion in this area.

House

- Training of Dental Students

  NIDR has participated with the NIH in preparing an announcement of plans to support such training as suggested by the Committee.

- Brittle Done Disease

  See narrative for Senate Directive in this area.

FY 1982 Program Changes

Major Activities to be Initiated in FY 1982

New Initiatives

Caries

- Survey of fluorosis and caries incidence in children residing in areas having greater than 1 ppm fluoride in the drinking water.
- Testing of caries prevention agents for self-application by adults.
- Studies of enamel remineralizing systems which appear to amplify the anti-caries effect of topical fluoride treatment.
- Research on the replacement of cariogenic micro-organisms in the oral flora with non-cariogens.
- Studies of environmental and dietary factors related to caries.
- Behavioral research concerning retention of children in caries prevention programs.

Periodontal Diseases

- Establish new specialized clinical research center for study of chemotherapeutic and preventive methodologies.
- Studies to develop diagnostic instrumentation.
- Clinical research training program in periodontal pharmacology.

Craniofacial Anomalies

- Long-term studies of acquired craniofacial defects to determine incidence, prevalence and severity and to identify and characterize sequelae and repair mechanisms.

Soft Tissue Stomatology and Nutrition

- Basic and clinical studies related to immunization against viral infections.

Restorative Materials

- Studies to develop improved dental diagnostic methods.

Pain Control and Behavioral Studies

- Intervention studies to enhance acceptance and practice of preventive dental disease measures.
- Multidisciplinary studies of chronic pain.

Intramural

- Major expansion in clinical and associated laboratory reseach activities, including facilities renovation for Clinical Center-North Corridor.

Expansion of Ongoing Activities

Caries

- Field evaluation of various clinically-tested fluoride-based techniques.

Periodontal Diseases

- Expand support for pharmacologic studies and human clinical trials.
- Research to develop a controlled-release system for antimicrobial agents.

Craniofacial Anomalies

- Studies to define alterations in the neuro-muscular patterns of activity associated with craniofacial disfigurement.

Soft Tissue Stomatology and Nutrition

- Research on the etiology and prevention of oral ulcerative diseases.
- Research on bone biology.
- Training for nutritional research related to oral diseases.

Restorative Materials

- Expansion of tooth implant clinical trials.
- Re-institution of clinical trials of new materials for maxillo-facial prostheses.

Pain Control and Behavioral Studies

- Research on dental anesthesia and sedation.
- Research on central nervous system pain control mechanisms.
- Intervention studies to alleviate dental fears and anxieties.

Dental Research Institutes and Centers

- Expansion of clinical research programs.

Intramural

- Restore basic research activity and expand clinical research activities.

Potential Impact of Program Changes on Period FY 1982-1984

Caries

- Fluorosis studies, adult clinical trials, studies on enamel remineralization and replacement of oral microflora, epidemiological studies, and behavioral research will require additional funds in FY 1982, while additional field testing will require further increments for the above named initiatives.

Periodontal Diseases

- In order to establish one new specialized clinical research center, to support controlled-release studies, research on instrumentation, and to initiate training in pharmacology, additional funds will be needed in FY 1982, FY 1983, and FY 1984.

Craniofacial Anomalies

- New research on acquired facial disfigurement and expanded research on neuro-muscular activity associated with craniofacial disfigurement will require additional funds in FY 1982, FY 1983, and FY 1984.

Soft Tissue Stomatology and Nutrition

- To initiate new research on immunization against viral infections, to expand research on oral ulcerative diseases, bone biology and training in nutrition, the program will require additional funds.

Restorative Materials

- Programs in tooth implantology, clinical trials of maxillofacial prostheses and research on dental diagnostic technologies will require gradual increases in support to maintain present activities.

Pain Control and Behavioral Studies

- To maintain FY 1981 projects and to continue them into FY 1982 as well as to initiate new efforts related to intervention studies and research on chronic pain, additional funds will be needed.

Dental Research Institutes and Centers

- To implement a planned expansion of clinical programs in FY 1982, and to continue that effort, significant increments of new funds will be necessary.

Intramural

- A major expansion of clinical research and restoration of basic research activity will require additional funds.

Summary of NIDR's Research Plan Review Session with the Director, NIH

Caries Research and Health Promotion Activities

Research to develop a vaccine against caries has produced exciting results. Human volunteers who have ingested extracts of *Streptococcus mutans* show a significantly increased level of antibody to the bacteria in their saliva; however, the elevated antibody level was found to persist for only two weeks. Consideration is also being given to further development of a vaccine against bacterial glucosyltranferases, which has been shown to induce an effective response in non-human primates.

Other research emphases in caries include the following:

- Basic studies in rodents on non-cariogenic organisms which could be introduced into the mouth to compete with cariogenic organisms.
- Fundamental research on the role of cell surface receptors and chemotactic responses of bacteria in plaque formation, with the eventual goal of discovering chemical agents capable of disaggregating the plaque.
- Clinical tests on the use of an intra-oral device for slow release of fluoride, and planning for the first phase of a clinical trial. These devices promise to be particularly helpful to the 40% proportion of the U.S. population which has no access to a fluoridated water supply.
- Special testing procedures to measure the cariogenic potential of particular foods. The test results will be used to classify foods. This effort will augment the Institute's activities to educate the public about dental health.

Caries Educational Activities

NIDR is continuing to build its rather vigorous new program of public education on dental health topics. This is a commendable program which, together with the community demonstrations of special fluoride techniques for children, constitutes a significant service to the public at a very reasonable cost to the Institute.

Clinical Trials

The Institute has reconsidered the plans for a large-scale clinical trial on dental implants. The Institute has determined that it may be wise to wait for a year or two, examine the early results of a similar Veterans Administration trial, and then determine whether complementary studies are necessary to evaluate fully the efficacy and safety of dental implants.

The NIDR Board of Scientific Counselors has reviewed the evidence for a recently publicized self-help treatment of periodontal disease, which has been offered as an alternative to surgical treatment. The Board has judged that the technique shows enough promise to warrant a formal clinical trial. A proposal for such a trial, with applicable cost estimates, will be prepared in the near future.

Other Research Opportunities

The Institute recognizes the following important research opportunities:

- Long-term epidemiologic studies of the occurrence of acquired craniofacial defects. Funds may not be available for these studies until FY 1982.

- Studies of pain control substances produced by the central nervous system. NIDR is making efforts to encourage research in the field.

Stabilization of the Science Base

Reservations were expressed about the stabilization initiative, particularly for sustaining a fixed number of project grants within a constrained Institute budget. Under such conditions, the NIDR would maintain the total number of research project grants at the current level, but could not stabilize the number of competing research project awards because of a pronounced irregular cycling in its competing level. NIDR also would propose to protect other Science Base elements of its programs in addition to research project grants, particularly the intramural research activities.

In order to implement these stabilization measures within a tight budget, NIDR would suffer a decrease primarily in support for contracts, affecting many contracts for activities in the Applications area, including clinical trials.

If stabilization would proceed within a tight budget beyond the point of exhausting contract funds, individual and institutional training support would be reduced next, while center grants and research career awards would be maintained at a constant dollar level.

Stabilization could prove difficult for NIDR if it would require fixing the number of competing research project awards at a set level. The Institute would favor awarding as many competing grants as possible in 1981, although it is the high point of the cycle, and would seek to stabilize by augmenting the number of awards in the two low years. This would require additional resources in 1982 and 1983.

Centers

NIDR is supporting five Dental Research Institutes and Centers (DRI's) at a level of about $1.5 million each, and three Specialized Clinical Research Centers on Periodontal Diseases (SCRC's) at a level of about $565,000 each. At present, they conduct largely fundamental research and NIDR classifies them within the Science Base; funding has had to remain essentially level for the

last five years. Efforts are being made to encourage the DRI's to increase clinical research and clinical training, but this may be difficult to accomplish without additional funds.

Intramural Program

Now that a new Clinical Director has been appointed, the Institute plans to expand its clinical research programs. NIDR would like to establish a pain clinic in the Ambulatory Care Research Facility, to conduct studies in collaboration with NIMH, NIAMDD and NCI. It is estimated that ten additional intramural staff members will be required.

Training

NIDR is concerned about the continuing trend of contraction in support for training of dental research personnel. Professional categories experiencing shortages include epidemiologists with dental backgrounds, cariologists, investigators in socio-dental sciences and experts in clinical trials.

One of the NIDR Council members suggested that the concept of Federal/State matching funds be applied to research training grants. This idea should be raised for discussion at a meeting of the Coordinating Committee on Manpower Development.

Consensus Development Conference on Removal of Third Molars

The Consensus Development Conference on Removal of Third Molars, held in November 1979, produced agreement on a number of issues and resulted in numerous recommendations for futher study. No consensus could be reached on the issue of removal of partially or fully impacted third molars showing no evidence of disease. A short summary of the results is available from the NIH Office for Medical Applications of Research.

Follow-up on Evaluation Review Session

- A program evaluation of the National Caries Program has been completed. The Program was found to have achieved significant accomplishments, particularly within the research strategy area of combatting the microbial agent. However, it was judged that more emphasis is needed in two other strategy areas--dietary/nutritional aspects of caries, and improving delivery and acceptance of preventive methods. Other recommendations included the need for centers of caries research and training and a number of changes in the organization and management of the National Caries Program.

- A Request for Proposals has been developed for an evalution of the Craniofacial Anomalies Research Activities. It is expected that a contract for conducting the evaluation will be awarded during FY 1980.

Major Civil Rights and Affirmative Action Initiatives

The proportion of women and minorities employed under the Staff Fellowship program and Summer Employment program has grown in the past year. Affirmative action in a number of professional categories has been limited by slow growth in the number of minority and female dental students and applicants to dental schools. Notably, NIDR has achieved representation of 29% minorities and 35% women on its advisory boards.

On behalf of the National Advisory Dental Research Council, Drs. Wallace Mann and Gunnar Ryge participated in the review.

Chapter 8

NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES

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Chapter 8

NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES

Director's Preface

Significance of Environmental Health Problems

The major public health issue today, in terms of both morbidity and mortality as well as economic cost to society, is that which results from the people's interaction with their largely chemical environment. These exposures may result in severely disabling or fatal illness, interference with the reproductive process, or modification of our genetic inheritance. Thus, toxic effects resulting from such exposures can be manifested across decades or even generations.

In both human and economic terms the cost of environmental disease is enormous. It is a cost our society can ill-afford to pay if we are to maintain the vitality of our people while reducing the escalation in the cost of medical care.

Environmental health problems have three common features:

1. Due to inadequacy of the existing science base, frequently we do not know what action to take to control or to prevent environmental health problems.

2. Due to the lack of appropriate regulatory action, we cannot be assured that these problems are being contained at even their current proportions. In some areas the problem is less bleak, but with regard to the major problem of toxic dumps the situation may well not be even stabilized for several years.

3. Public health theory and practice ill prepare us to cope with the variety of individual human health problems arising out of toxic environmental exposures.

Without major increases in the science base we cannot expect that either our regulatory activity or our public health practice will improve significantly. Thus, the National Institute of Environmental Health Sciences (NIEHS) focuses its basic and applied resarch programs on the health issues emerging from our environment. It seeks to provide the new knowledge required to reduce the health hazards associated with exposure to toxic chemicals in our environment.

Strategy for Dealing with Environmental Health Problems

In order to develop the knowledge required to deal effectively with these problems, the NIEHS has established a variety of program efforts:

- Intramural and extramural basic and applied research.
- Test method development and testing activities committed to the National Toxicology Program.
- Development of research resources.
  - -- Environmental health sciences and marine centers
  - -- Expanded intramural research facilities
  - -- Expansion of ongoing training programs and development of new approaches to provide an increased research manpower pool.

In addition, the NIEHS continues to work toward better definition of environmental issues so that research programs can be developed to respond to those issues.

However, even before we get a firm grasp on the problems associated with determining the toxicity of single compounds, we are confronted with the enormously difficult task of determining the toxicity of two or more compounds acting in combination. The need to develop the knowledge required to deal adequately with the problem of chemical mixtures, and to develop understanding of the fundamental mechanisms of chemical compounds demonstrates the need for additional resources. To develop the knowledge required to cope with these major health issues, laboratory research and testing, as well as epidemiological investigations, are essential.

Goals

In order to develop strong interconnections among research, public health practice, and regulation, the NIEHS is an active partner in the National Toxicology Program and the DHHS Committee to Coordinate Environmental and Related Programs. It is through these mechanisms, as well as related ad-hoc and emergency activities, that the NIEHS maintains its focus on the broad health objectives of disease prevention. It is also through this effort that, in time, NIEHS programs will aid in reducing the disease burden caused by toxic chemicals in our environment and in restraining the increase in health care costs.

FY 1981 Program Changes

Major Activities to be Initiated in FY 1981

None.

Major Initiatives to be Maintained in FY 1981

During 1981 the NIEHS will continue the activation of its permanent facilities, which was begun in 1979. Many of the ongoing NIEHS research programs will be relocated into the new facilities. However, there will be no growth in the intramural program because of the need to utilize staff increases in the 1981 budget request to provide support staff necessary for activation and operation of the new facility.

While no increases will be provided for intramural research, the Institute will expand commitment to the National Toxicology Program through research contracts. At the same time, in the Institute's extramural research programs, there will be major increases only in the amount committed to funding prior year non-competing research grants.

Major Activities to be Cut Back, Eliminated, or Not Started in FY 1981

The overall impact of the FY 1981 budget request is mixed in terms of the Institute's continued development. Budget increases will be used to fund the increased numbers of non-competing research grants, to fund NIEHS contract activities in the National Toxicology Program, and to activate the permanent facility with no increase in research programs. Thus, the following overwhelming needs are not addressed:

- The need to take advantage of the research opportunities afforded by the new facility;
- The need to maintain orderly growth in the research grants program;
- The need to increase the number of Institute-supported centers; and
- The need to expand the number of individuals in training for careers in environmental health research.

Impact of FY 1980 Congressional Directives Upon FY 1981 Plans

The House directed the Secretary, HHS, to develop a five-year plan for the NIEHS that would lay out the schedule for the activation of the new Institute facility, the program plans for the Institute, and the staffing and budgetary requirements to carry out these plans. The Senate directed the Institute to prepare a similar plan. The NIEHS participated in the development of the HHS plan sent to the House and prepared the plan submitted to the Senate. The out-year projections of the Senate report have been factored into the Institute's program planning for FY 1981 and beyond.

FY 1982 Program Changes

The major program changes projected in FY 1982 will be in four major areas:

1. Broad scale activation of the permanent facilities;
2. Increased support for extramural research projects;
3. Enlarged research manpower development programs; and
4. Significant expansion in the Institute's commitment to the National Toxicology Program.

Permanent Facilities

The major planned program changes flow from activation of the Institute's permanent facility. In 1982 the Institute will occupy new government-designed and owned facilities. With the currently available leased facilities and the new facilities, NIEHS will have the most advanced laboratories available for environmental toxicology. The increased facilities, in conjunction with the Institute's extramural programs, will permit the development of full research programs in the major areas of importance to the Institute. Thus, the Institute will have the capacity to develop many of the research programs needed to attack the problems left unresolved from the past, and those new ones which undoubtedly will emerge in the years ahead.

In the coming years, particular emphasis will be placed on:

- Learning more about and describing the basic mechanisms through which toxic agents express themselves;
- Learning more about the toxicity of chemicals either already in the environment or proposed for introduction;
- Learning more about interactions of chemicals in order to attack such problems as those dealing with hazardous waste; and
- Developing better laboratory tests to assess health hazards to the human population.

To meet these challenges, the Institute plans to fully develop those intramural programs that have already been developed on a restricted basis. Among the areas to be brought to maturity in the permanent facilities are behavioral and neurological toxicology, chronic organ toxicity, comparative pathology, chemistry, reproduction and development, physical factors and molecular biophysics, pharmacokinetics, and comparative biology. The areas of genetic risk assessment, genetic monitoring, genetic testing, and toxicity bioassay all will receive special emphasis because of their importance to the successful implementation of much of the recent environmental legislation aimed at the protection of human health, such as the Toxic Substances Control Act. Beyond these important areas there is a continuing urgent need to develop better means for assessing the health risks associated with exposures to toxic chemicals. The Institute is continuing its efforts in this area.

Extramural Program

In the extramural component of the Institute's programs, there are four major program areas. These are:

1. Prediction, detection and assessment of environmentally-caused diseases and disorders.
2. Mechanisms of environmental diseases and disorders.
3. Environmental health sciences and marine centers.
4. Training.

The Institute is planning a series of studies that it hopes will yield a better assessment of specific manpower needs for the years ahead. In addition, by providing funds to increase the number of new research grants the Institute is able to support, the 1982 plan will regain the program development momentum lost in the 1981 budget. The 1982 plan also projects continued expansion of this program. This is critical if the Institute is to strengthen the science base in the field of environmental health. Specific plans for the extramural program areas follow.

Prediction, Detection, and Assessment and Mechanisms of Environmentally-Caused Diseases and Disorders--Research areas that have been identified for special emphasis include: physical factors and, in particular, ionizing and non-ionizing radiation; effects of environmental agents on the endocrine system, digestion, and nutrition; synergistic and additive effects of smoking; effects of environmental agents upon the immune system; and development of rapid, reliable, and inexpensive tests for toxicity in response to the National Toxicology Program.

That part of the program which deals with prediction, detection, and assessment of environmentally-caused disease and disorders will address the above emphasis areas by attempting to identify and determine the nature, location, and extent of the environmental pollutants that affect each physiological system, and to determine the nature and extent of the exposed population. Moreover, it will be important to understand the interaction of the various pollutants with each other, the biological processes, and the manner in which the various agents impinge upon or interct with biological systems. The knowledge gained through the understanding of one system may provide predictive capabilities for the action of similar environmental agents operating in a like mode.

Additional efforts will be made to develop and improve the methods for sampling and analysis of pollutants by development of more sensitive measuring devices and sampling techniques. In accordance with the National Toxicology Program needs, a concerted effort will continue to be made to encourage the development of rapid, reliable, and inexpensive tests for toxicity for representative environmental pollutants.

Recent studies have demonstrated a possible effect of certain environmental contaminants upon the immune system in animals and humans. The extent of this phenomenen in nature is entirely unknown, as is its significance with respect to health effects. Efforts will be intensified to develop an understanding of the relative importance of a variety of environmental agents on the immune system.

The changing nature of the types and levels of environmental pollutants resulting from alteration in the country's energy usage will necessitate an increased emphasis on synergistic and additive effects. Studies will center upon physiological systems involving digestion, nutrition, and the endocrine system.

The areas of emphasis already discussed also will serve as a focus for mechanism studies. This approach should save time and effort in the study of environmentally-caused disease through providing knowledge of how and why toxic agents cause injury. Mechanisms of toxicity also can be used to develop

methods for detecting injury in early and reversible stages; and an understanding of the disease process can lead to avoiding, changing, or possibly correcting the condition that may lead to the damage.

An understanding of the biochemical and biological mechanisms of disease production lends itself not only to control and prevention, but also to prediction of the relative susceptibility of people at high risk by virtue of their genetic background, nutritional status, or pre-existing disease state; to improved prediction of long-term chronic effects; to development of sensitive assay systems; and to improvement in the reliability of dose-effect extrapolation from animals to humans.

Environmental Health Sciences Centers--The ultimate goal of research in the environmental health sciences is disease prevention. Toward this end, the nine operative EHS centers will continue current research programs in areas that parallel and complement both the NIEHS intramural research programs and research being supported under the regular research grants program. Plans are being developed for clinical studies on a variety of environmentally-related diseases, inhalation toxicology, and radiation in combination with chemicals in the induction of mutations and cancer.

Marine and Freshwater Biomedical Centers--These centers are located at independent or university-affiliated marine or freshwater laboratories. In all of the centers, particular emphasis is placed upon marine and freshwater organisms as models for assessment and prediction of biological (particularly human) effects of toxic environmental chemicals and physical factors. Appropriate steps are taken in the establishment of these centers to avoid duplication of thrust and emphasis so that a balanced program is attained that is consistent with the identified research needs and priorities of the Institute. New centers will be established on an irregular schedule as good, relevant applications are received.

Manpower Development

The NIEHS training program provides trained scientific personnel to conduct research programs supporting the mission of the Institute. The mechanisms for support of this manpower development are institutional NRSAs, supporting both preand post-doctoral training, and individual NRSAs, composed of post-doctoral fellowships and senior fellowships. This training takes place at institutions with existing expertise in toxicology, mutagenicity, pathology, and epidemiology and bio-statistics. Due to the consensus about the urgent need for additional individuals with research training in these areas, the NIESH training budget has been in a growth phase since 1976, the year of the passage of the Toxic Substances Control Act. In 1982 NIEHS will continue its initiatives to stimulate development of new programs to train in all of the aforementioned areas, with specific emphasis on toxicology and epidemiology.

The needs for these researchers have, until now, been documented rather subjectively. By the end of 1981, a contract let in 1979 will be completed that will provide information specifically indicating the types of existing needs and existing training programs in environmental toxicology. This information will be used to guide future program growth efforts and to evaluate the current support thrusts of the NIEHS in this area.

National Toxicology Program

The Institute projects an increase in its resource commitment to the National Toxicology Program (NTP). A summary of the Director's Review Session on the NTP is provided in the trans-NIH section of this document.

Potential Impact of Program Changes on Three-Year Period (1982-1984)

The year 1982 will be the first year of significant implementation of the program plans laid out for the Institute over a decade ago. While further and continuing developments in science, technological development, industry, and society have served to modify the specifics of those plans, in their broad outlines they remain valid. The fundamental changes in these plans center on the National Toxicology Program; and even here it represents basically only a change in program emphasis and better integration of research efforts conducted in four different research organizations. What remains unchanged is the continuing need for a major national effort to develop the knowledge necessary for understanding how and to what extent human health is adversely affected by the environment.

Summary of NIEHS' Research Plan Review Session with the Director, NIH

NIEHS Permanent Facility

The new permanent facility will be ready for occupancy by the end of the summer of 1981. Together with the leased build- ings now in use, these new facilities will give the NIEHS a truly outstanding laboratory for environmental health studies. All of the new positions requested by the NIEHS for FY 1981 would be used to activate and operate the new facilities. It appears that a sequence of problems has caused delays which will have an adverse impact on total construction costs. Although it is difficult to estimate the total financial impact of these problems, the sum could be substantial.

Stabilization of the Science Base

The NIEHS, a relatively young Institute, has not yet achieved the science base necessary to permit an adequate response to the growing pressures to provide the knowledge upon which effective regulation and control of environmental hazards can be based. Consequently, some growth in the science base is required to sustain the momentum which has been developed through prior investments directed toward the establishment of a critical mass in the environmental health sciences.

Centers

The NIEHS provides core support for two types of centers--Environmental Health Sciences Centers and Marine and Freshwater Biomedical Centers.

Support will continue for nine Environmental Health Sciences Centers to facilitate multidisciplinary research on environmental health problems. The centers supported by these grants fill critical needs in the national environmental health research effort that cannot be met by individual research projects or less formal or short-term collaboration. Each of these centers has a different primary thrust and problem orientation. Overall, they serve as a coordinated national resource for research and manpower development in the environmental health sciences.

The NIEHS will continue to support six Marine and Freshwater Biomedical Centers. These centers are located at independent or university-affiliated marine or freshwater laboratories. The centers focus multidisciplinary research on marine and freshwater organisms as model systems for elucidating mechanisms of toxicity of environmental agents. The rationale for use of such models is the universality of many basic biochemical processes in living systems and the fact that initiation of pathologic damage induced by toxic substances in man is often reproducible in the simple organs and tissues of lower organisms. In addition, because of their vital role in the food chain, and because many environmental agents become concentrated in both fresh and salt water species, marine and freshwater research is a vital component of the study of the health effects of the environment.

Intramural Program

Because of the immediate need to utilize personnel increases to provide staff support for the activation and operation of the new permanent facility, only small increases will be provided for intramural research in FY 1981. However, the new facilities will permit the full development of many promising intramural research programs in future years. Particular emphasis will be placed on:

1. Studying and describing the basic mechanisms through which toxic agents express themselves.

2. Learning more about the toxicity of chemicals either already in the environment or proposed for introduction.

3. Examining interactions of chemicals in order to attack such problems as those dealing with hazardous waste.

4. Developing better laboratory tests to assess health effects in the human population.

Review of Second Task Force Report for Planning in Environmental Health Sciences

A Planning Work Group was convened to review the Report of the Second Task Force for Research Planning in Environmental Health Science and make recommendations regarding research areas of particular relevance and importance to the NIEHS. The NIEHS concurs in most of the recommendations of the Planning Work Group.

When its recommendations are viewed as a whole, it is clear that the Planning Work Group sees the proper role of the NIEHS as one lying across the entire continuum from basic research to applied research to application, with the emphasis on applied research. This is consistent with the way the NIEHS programs have evolved over the last decade.

Civil Rights and Affirmative Action Initiatives

The Institute's EEO Coordinator has developed an Affirmative Action Plan. It is encouraging to view the progress that has been made in the training of supervisory and management personnel. Of the supervisors and managers identified for training, 44 have completed such training and 11 are currently enrolled.

National Toxicology Program

The Secretary has approved the second annual plan for the National Toxicology Program (NTP). The NTP has shown, in its first year of operation, that it will indeed provide an effective mechanism for integrating the toxicology research and testing activities of the relevant HEW research agencies

in order to strengthen the science base underlying toxicology testing and to better provide needed information to regulatory agencies. It is clear, however, that the current organizational arrangement does not provide the stability that is necessary for long-range planning and sound program development. It is important to begin now to consider alternative corporate structures for the continued development of the NTP.

Dr. Norton Nelson, consultant to the NIEHS Advisory Council participated in the review session. His insights contributed greatly to the discussion.

Chapter 9

NATIONAL EYE INSTITUTE

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Chapter 9

NATIONAL EYE INSTITUTE

Director's Preface

Significance of the Health Problem

Over 10 million people in the United States are affected by visual impairments which are not amenable to further improvement with corrective lenses. Each year, over 3.7 million new cases of eye disorders are diagnosed, and approximately 2 million eye injuries occur. Eye disorders are outranked only by arthritis and cardiovascular diseases as a leading cause of limited activity among persons 65 years of age and older.

The total cost of visual disorders and blindness to our nation is now estimated at approximately $8 billion per year in direct health care costs and in indirect costs associated with lost income and disability payments.

Most blindness and visual disability in the United States is caused by congenital, vascular, or degenerative disorders of the retina, examples of which are retinitis pigmentosa, diabetic retinopathy, and senile macular degeneration. No means of prevention or cure exist for most retinal diseases, although impressive progress has been made in preventing blindness from diabetic retinopathy thanks to research supported by the NEI. Other leading visual problems are cataract, glaucoma, uveitis, corneal infections and dystrophies, strabismus, and amblyopia. Although treatments are available for some of these conditions, most of those available leave much to be desired, and means of prevention are generally lacking.

Research Program Strategy

About 84 percent of the National Eye Institute's current and projected budgets supports development of the Science Base in vision research. About 86 percent of the NEI research grants budget supports investigator-initiated research through regular research project grants (ROIs). The NEI supports no program project grants.

Guiding the NEI's overall research program strategy is Vision Research--A National Plan: 1978-1982. This comprehensive plan is now being evaluated in terms of the numbers and kinds of research grants actually supported during these years. The National Advisory Eye Council's Program Planning Subcommittee has been recently reestablished, and plans are underway for a major updating and revision of the plan by December 1981. In the meantime, program announcements are being issued and workshops held to stimulate an increase in multidisciplinary efforts in several fields assigned priority in vision research.

The Institute's clinical research center award presently accounts for less than one percent of the extramural budget. However, because of numerous

opportunities identified for clinical vision research centers in NEI's comprehensive plan, we expect the number of centers to increase from 10 in FY 1980 to 17 in FY 1982 if sufficient resources are made available. Additional funding is essential, for the centers must not compromise the support for individual research project grants.

Clinical trials are becoming an increasingly important part of the NEI's research strategy. The NEI is now supporting 13 clinical trials, of which three are large-scale, multicenter projects funded by contracts and the rest either single center of multicenter trials supported by individual research project grants.

The new NEI construction grant program, authorized by the Congress in 1978, received its first appropriation of $3 million in FY 1980. Program guidelines have been developed in consultation with the National Advisory Eye Council.

Goals

The goals of the National Eye Institute are to improve the prevention, diagnosis, and treatment of visual disorders, thereby alleviating human suffering and reducing the expense of medical care and other social and economic costs. In considering the potential relevance of the above research strategy to achieving these goals, it is useful to review some of the accomplishments of the past decade to see how effective this strategy has been. Cataract extraction has become one of the safest and most successful of all major surgical operations. New antiviral and antibiotic drugs have revolutionized the treatment of ocular infections. Corneal transplantation has become highly successful because of improvements in tissue preservation and operating procedures and better assessment of prospective tissue donors and recipients. The course of diabetic retinopathy, virtually hopeless just a few years ago, is now being successfully controlled by two therapies, photocoagulation and vitrectomy. Although some of these advances have required the development and use of expensive medical technology, the savings in reduced hospital days and days lost from work, not to mention alleviation of pain, disability, and anxiety, have more than offset this added expense.

FY 1981 Program Changes

Major Activities to be Initiated in FY 1981

None.

Major Initiatives to be Maintained in FY 1981

Science Base

Retinal and Choroidal Diseases--One of the most important and exciting recent findings in vision research is that a deficiency in phosphodiesterase, the enzyme which metabolizes cyclic GMP, occurs in a form of retinal disease found in a strain of mice and in a strain of Irish setter dogs. This is the first time that a biochemical defect has been identified in the retina of animals with a disorder very similar to human retinitis pigmentosa, and it opens

the way to research directed at correcting the defect. In FY 1981, work on the dog model will be aimed at determining if the enzyme defect is the key event in the retinal degeneration or is a secondary manifestation.

A human condition similar to retinitis pigmentosa, gyrate atrophy of the retina, has been found to be associated with elevated serum ornithine in affected patients. The cause of the excess ornithine has recently been shown to be a deficiency in an enzyme which normally metabolizes this amino acid. A single patient, who has now been followed for 19 months on a diet low in protein and arginine (a precursor of ornithine), has shown significantly improved night vision and dark adaptation. Research on gyrate atrophy will continue in hope of determining if this diet can effect a permanent reversal of the eye condition.

Other retinal studies to be maintained are research on the interface between the retinal blood vessel wall and the retinal cells, an important factor in diabetic retinopathy and other vascular diseases, and on the role of cyclic GMP phosphodiesterase in the transduction of light stimuli into visual impulses. Tissue culture of retinal components, particularly pigment epithelial cells, will allow detailed in vitro investigation of normal and pathological processes underlying such disorders as senile macular degeneration, retinitis pigmentosa, and gyrate atrophy.

Corneal Diseases--It is now possible to study defects of corneal connective tissue which underlie corneal dystrophies in intact human corneas grown in tissue culture. By incubating corneas excised during transplantation under conditions that permit incorporation of radio-labeled precursors into structural macromolecules which are then extracted and analyzed, specific enzymatic defects have been identified, for instance, in macular corneal dystrophy. Pursuit of such studies in FY 1981 should lead eventually to development of rational, specific therapies and provide a sounder basis for genetic counseling.

Cataract--Preliminary trials of aldose reductase inhibitors, which have been used successfully to slow or prevent cataract formation in diabetic laboratory animals, were begun in diabetic patients in FY 1980 and will continue into FY 1981. In one study, the effects of an experimental inhibitor, alrestatin, will be measured in diabetic patients who have intermittently blurred vision during circadian cycles of hyperglycemia. If the visual acuities of these people improve, this would provide strong evidence of the role of the sorbitol pathway in the causation of diabetic cataracts as well as other, more common diabetic complications and possibly lead to a means of preventing them.

Having demonstrated that it is possible to isolate the enzyme inhibitor which causes hereditary mouse cataracts from the epithelial cells of a cataract grown in tissue culture, investigators will begin to use this approach to determine if there is an enzyme defect in human congenital cataracts as well.

Glaucoma--Basic studies on aqueous hydrodynamics will shift increasingly from animal to human research. Tissue culture of trabecular meshwork will be pursued in order to learn more about the function of the trabecular epithelial cells which regulate the flow of fluid out of the eye. Abnormalities in the trabecular endothelium may be the primary cause of obstructed aqueous outflow in open-angle glaucoma.

Sensory and Motor Disorders of Vision--Research on applying psychophysical testing to the diagnosis of retinal and neurophthalmic disorders will be emphasized. These techniques to measure psychological and behavioral responses to visual stimuli promise to afford more precise diagnosis of retinal and neurosensory disorders and help pinpoint the exact location and nature of the primary lesion in such diseases. It is possible, for example, to investigate the earliest changes in macular degeneration by measuring responses to stimuli from a very small area of the fovea within the macula and to dissect out the many steps in both normal and abnormal information processing in the retina.

Biometry and Epidemiology--A pilot study for a nationwide Visual Impairment Study will get underway in FY 1981. This is intended as a continuous, three-stage survey of visual impairment to measure the prevalence of visual impairment and legal blindness by cause; determine differentials in the prevalence of visual impairments according to age, sex, race, and other factors; measure trends over time in the prevalence of impairment; identify opportunities for case-control studies of disease etiology; and provide information for the planning of health services programs.

Applications

A clinical trial to evaluate the usefulness of both the argon laser and Q-switched laser as treatments for glaucoma will be initiated in FY 1981. Timolol, the new beta-adrenergic blocking agent for glaucoma, will continue to be evaluated to determine its long-term effects, its value in preventing visual field loss, and its interaction with other glaucoma drugs.

In addition, several other clinical trials, including the Early Treatment Diabetic Retinopathy Study, Diabetic Retinopathy Vitrectomy Study, and 12 other grant-supported trials begun in FY 1979 and 1980, will continue.

Transfer

A conference is planned to assess the state of the art in refractive keratoplasty (surgical manipulation of the cornea to correct refractive error), specifically whether one form, keratophakia, is safe and effective and whether it is a suitable alternative to intraocular lens implantation.

Training

Major objectives of training programs during the coming year will include: increasing the number of scientists committed to studying the lens of the eye; training new clinically oriented glaucoma researchers; research training in the nutritional aspects of ocular disease; and training scientists, especially clinicians, in biostatistics and epidemiology.

FY 1982 Program Changes

FY 1982 plans provide for increased support for regular research project grants, a modest increase in the number of clinical vision research centers, and additional funds for contracts to support new and continuing clinical trials and the nationwide Visual Impairment Study.

Science Base

Retinal and Choroidal Diseases--The discovery of a specific enzyme defect resulting in high levels of ornithine in the serum of patients with gyrate atrophy and of an enzyme deficiency in the photoreceptor cells of animals with an inherited retinal disease has set the stage for research in FY 1982 on the basic mechanism through which the retina is harmed by these biochemical defects. The recent discovery that there is a defect in the uptake of taurine in the platelets of people with retinitis pigmentosa is additional evidence that there may be biochemical defects associated with a number of other degenerative eye disorders.

There will also be opportunities to study autoimmunity in the eyes of laboratory animals and humans. Such investigations will focus on the antigens involved, genetics of the immune response, mechanisms of induction and pathology, and possible means of suppressing the response. In addition, attention will be directed toward the mediators that trigger inflammatory reactions in the eye and possible methods of suppressing them as well.

Studies of neurotransmitters in photoreceptor cells and other retinal neurons will be aimed at a better understanding of the neurochemical circuitry responsible for processing visual information in the retina. It is hoped that such studies will also lead to better understanding of retinal degenerations and of amblyopia.

Corneal Diseases--Animal studies have demonstrated the possibility of restoring clarity to opaque corneas in which only the endothelial layer is affected, the situation that occurs in most corneal dystrophies. In one technique, the damaged endothelial cells are scraped off and replaced with a sheet of new cells grown from vascular endothelial cells taken from the animal's own body. This kind of "autotransplant," if feasible in humans who would otherwise require a full thickness corneal graft from a donor eye, would eliminate both the problem of tissue availability and storage and the hazard of tissue rejection. Studies to assess the long-term outcome of such methods and explore the possibilities of clinical application will be pursued in FY 1982.

Cataract--There is now evidence that the terminal stages of human senile cataract, in which there is abnormal aggregation of insoluble protein molecules and accelerated protein degradation, may be very similar to the final stages of experimentally induced cataracts in animals, even though the initiating event is quite different. Therefore, animals with diabetic or congenital cataracts may be suitable models for evaluating agents which may be capable of interfering with the development of incipient cataract regardless of the etiology. Research in this area is expected to expand in FY 1982.

Glaucoma--There is still no clear understanding of the relationship between ocular hypertension and subsequent development of the retinal changes and resultant visual field losses characteristic of glaucoma. Studies of affected and adjacent nonaffected retina following a detailed protocol are planned with the aim of determining the earliest abnormalities in retinal function and to develop therapies directed toward preventing further visual field loss or in slowing the rate of development of abnormalities in aqueous humor dynamics.

Sensory and Motor Disorders of Vision--The exciting possibility of reversing the effects of amblyopia by drug therapy is suggested by recent work showing that bicuculline will reactivate 60 percent of visual cortical cells previously rendered inactive by monocular deprivation in the cat. Although it is much too early to explore the clinical implications of this work, it has broad significance in neurophysiology. It might, for example, lead to a better understanding of neuronal inhibition, and it adds significantly to evidence that physiological alterations of the visual system, induced by visual deprivation during critical developmental periods, are not necessarily permanent. Research in this field in FY 1982 will focus on finding more effective, longer lasting, and less toxic pharmacological agents than bicuculline and on developing better experimental models of amblyopia.

Intramural--The move of the NEI's Laboratory of Sensorimotor Research to the Ambulatory Care Research Facility in FY 1982 will facilitate collaboration with the NEI's Clinical Branch on transferring of basic knowledge in neurobiology to clinical problems. Initial emphasis will be on studying the focal electroretinogram in patients with various retinal diseases to pinpoint the site of the primary lesion, and on analyses of oculomotor and vestibular physiology. An attempt will then be made to correlate anatomical with physiological and behavioral observations.

Biometry and Epidemiology--The Visual Impairment Study will be fully launched with the awarding of contracts to support data collection in 15 U.S. Standard Metropolitan Statistical Areas.

Applications

Phase-out of the Diabetic Retinopathy Study will be completed and marked by publication of papers on the natural history of diabetic retinopathy, details of risk factors, and the effects of laser treatment on macular edema. The Early Treatment Diabetic Retinopathy Study will continue.

Transfer

By FY 1982, five current clinical trials, the Diabetic Retinopathy Vitrectomy Study, Macular Photocoagulation Study, Ocular Histoplasmosis Study, Branch Vein Occlusion Study, and the Role of Vitamin E in the Treatment of Retrolental Fibroplasia, are expected to have generated results which will be ready for broad dissemination to practitioners and patients. Accordingly, the NEI plans a major effort to insure that the studies' results are widely known and understood.

There will also be a task force on ocular melanoma to explore the most appropriate means of diagnosing and treating this important form of ocular cancer and to identify research initiatives for the future.

Summary of NEI's Research Plan Review Session with the Director, NIH

Your presentation conveyed the excitement of the field of vision research, described the potential for further advances, and underscored the challenge inherent in building upon the base of laboratory and clinical research investigations assembled over the last decade. The insights and perspectives of your Advisory Council members, Drs. Duane, Brown, and Christensen, who attended the session contributed greatly to the discussion.

Vision Research: Progress and Prospects

In its ten-year history, the National Eye Institute has undergone steady program expansion in terms of funding, increased diversification of program mechanisms, and rapid developments in the field of vision science. The NEI budget has grown from $23 million in FY 1970 to $113 million in FY 1980. Over this same period, the number of research grants supported by the Institute has risen from 167 to 1,011. A combination of factors has contributed to this growth and exerts pressure for its continuation. One important factor is the unique opportunity the visual system offers as a model for research in diverse areas. Among the advantages of the eye as a research model are that the input and output of the system can be measured with great precision, and much of its morphology, physiology, and pathology can be evaluated in vivo. Such advantages have attracted many high-quality investigators to this field who have helped place vision research directly in the mainstream of biomedical research and at the frontiers of some of the most rapidly developing scientific disciplines. Our discussion of some of the past and potential advances in vision research indicated the following:

- The visual system serves as the research model for many investigations being pursued in neurobiology. NEI's interest in this field includes studies of neurotransmitters in the visual system. The Institute has made a significant investment in neurobiology, and work in the visual system has laid the groundwork for a substantial portion of the new techniques and insights that have been developed in the neurosciences.

- Expanded use of the visual system is also occurring in cell biology; for example, investigators are recognizing the unique properties of the lens to pursue studies of cell metabolism and membrane biochemistry.

- Clinical trials have become an important part of the NEI research portfolio. The Institute is now supporting 15 clinical trials, of which three are large-scale, multicenter projects funded by contracts and the rest either single center or multicenter trials supported by research grants. Approximately one-third of the 102 departments of ophthalmology in the United States are now involved in one or more clinical trials; ten years ago, none were.

NEI Planning Process

The Institute is to be commended for the development of a highly structured and innovative planning process which has proved a useful mechanism to foster consensus among the vision research community, to guide decision-making

by Council, and to communicate program needs to the Congress, Administration, and the public. Two comprehensive vision research plans have been developed under the auspices of the National Advisory Eye Council--the first was published in 1975, and the second, which outlines research opportunities, program needs, and priorities for the period 1978 to 1982, was completed in 1977. The latter plan specifies the number of grants that will be required in various problem areas to take advantage of the research opportunities identified. For FY 1982, this number is 1500 research project grants. The Institute, in concert with the National Advisory Eye Council, has now initiated a third planning cycle.

Program Mechanisms

- Research Project Grants. NEI does not support program projects. Approximately 88% of the current NEI extramural budget is allocated to research project grants. In FY 1980, it is estimated that 36% of approved, competing research projects will be funded.

- The Institute has developed innovative approaches in adapting NIH support mechanisms to program needs. Two examples were cited. The Cooperative Cataract Research Group (CCRG) was formed several years ago in response to a proposal from several investigators. In the CCRG, NEI provides funds through the regular project grant mechanism to about 40 independent investigators participating in a cooperative program to promote and facilitate research on the human lens and cataract. An analogous approach is used to support the cooperative activities of the independent investigators who constitute the National Eye Tracker Group which was established to ensure orderly development and access to a relatively expensive, noninvasive technology which has proved important to study of the retina, visual nervous system, visual perception, and ocular musculature.

- Centers. The NEI currently awards core grants (P30) and specialized clinical research center grants (P50) and, if new monies are made available, will initiate a new developmental clinical research center award (P20) in 1982.

(1) Core grants. In FY 1980, NEI plans to provide core grant support to 23 institutions at a total funding level of $4.2 million. Funds are provided for shared resources, facilities, and services in support of both laboratory and clinical research. Grant funds may be used to pay support staff salaries and that portion of the program director's salary attributable to center activities. Last year, the average amount of support per core grant was $187 thousand. In order to qualify for core support, an institution must have at least six research grants active in the program proposed for support and at least four independent investigators working on them. Using these criteria, an estimated 25 additional institutions would now be eligible to apply for NEI core grants. The number of grants and the relative proportion of NEI research grant dollars attributable to core support have risen substantially since the awards were first made about six years ago. Therefore, NEI, in conjunction with its Council, is reexamining the role of this mechanism in the Institute's programs.

(2) Specialized clinical research centers. Currently, seven centers are being supported. The number funded has decreased substantially over time because many former centers have not fared well in recompetition. Support is provided for collections of individual projects, which can only be carried out within a clinical research center setting, and for associated resources.

(3) Developmental clinical research centers. The purpose of this proposed award is to strengthen the clinical research capabilities of vision research institutions. The award would provide up to five years of one-time, nonrenewable support. Additional funds would be needed so as not to divert support from research project grants.

- Research and Development Contracts. About 98% of NEI contracts are used to support fixed protocol clinical trials and the remainder to develop and maintain specialized research resources. In FY 1980, contract funds are estimated at $6 million.

- Intramural. The Institute is preparing for the move of its Laboratory of Sensorimotor Research to the new NIH Ambulatory Care Research Facility in FY 1981. This should provide some alleviation of the Institute's space problems.

- Construction. The Institute has received an appropriation of $3 million (available until expended) for the vision research facilities construction program authorized by a 1978 amendment to the Public Health Service Act. Awards would be made as soon as possible after completion of peer review of the applications, possibly between May and September 1981.

Stabilization of the Science Base

Highlights of our discussion concerning the proposal to stabilize NIH support of the science base were as follows:

- Given the high proportion of the NEI budget allocated to research project grants, a proposal which would regulate this support mechanism could significantly reduce program flexibility and impair the ability of the Institute to adjust the mix of program mechanisms to take advantage of new opportunities as they emerge.

- Under restrictive budget conditions, coupled with a requirement to stabilize the support of research project grants, the alternatives open to the Institute are limited by two factors. First, in the Institute's view, it is essential that the funding rate for approved competing research project grants not drop below approximately 33%. Second, the amount of funds that could be made available through cutting back support for noncompeting grants is limited in that grant budgets are already being stringently evaluated both by study sections and Institute staff, often resulting in reductions of 25 to 30% from the original request. Furthermore, approximately 70 to 75% of most grant awards support personnel costs, which are extremely difficult to reduce. If it were necessary to reduce support for noncompeting R01s, this would

be done selectively based on the priorities identified in the NEI program plan and in consultation with representatives of the vision research community.

Research Highlights

Our discussion touched upon the following promising new developments and research initiatives:

- Corneal Diseases. One of the most promising vision research approaches over the past few years has been the laboratory culture of normal and diseased cells from ocular tissue. One new tissue culture technique has the potential for permitting repair of damaged corneas where only the endothelial cell layer is affected, by scraping the damaged cells off the cornea and replacing them with a sheet of normal endothelial cells grown in the laboratory. This technique has been applied successfully in animals, and investigators are now working on methods for growing human corneal endothelial cells.

- Retinal Degeneration. For the first time, a biochemical defect has been identified in the retina of animals with a disorder very similar to human retinitis pigmentosa, opening the way to research directed at correcting the defect.

- Cataract. Preliminary trials of aldose reductase inhibitors, which have been used successfully to slow or prevent cataract formation in diabetic laboratory animals, have begun in diabetic patients. The pharmaceutical industry is now developing additional compounds which can inhibit this enzyme.

- Sensory and Motor Disorders of Vision. The possibility of reversing the effects of amblyopia by drug therapy is suggested by recent work in the cat showing that bicuculline will reactivate 60% of visual cortical cells previously rendered inactive by monocular deprivation. This has broad significance in neurophysiology.

- Biometry and Epidemiology. Patient recruitment for the Early Treatment Diabetic Retinopathy Study recently began. The purpose of this clinical trial is to evaluate the effectiveness of argon laser photocoagulation and aspirin therapy in delaying or preventing progression of early diabetic retinopathy to more severe stages. Twenty-two university medical centers are cooperating in the trial; 4,000 patients are expected to participate; the data collection phase is expected to last at least five years; and the FY 1981 cost is estimated at $4 million. It was also noted that a number of important questions have been raised concerning the use and long-term effects of intraocular lenses; some of these questions are amenable to resolution through a controlled clinical trial the costs of which are estimated at $1 million for the first year. The number of lens implants continues to increase rapidly. The OD encourages the Institute to discuss with the Health Care Financing Administration the possibility of its providing financial support for such a trial.

In FY 1981, NEI is proposing to initiate a pilot study for a nationwide survey of visual impairment and its causes that will be undertaken in conjunction with the National Center for Health Statistics and the Bureau of the Census. NEI plans a continuous, three-stage survey to measure the prevalence of visual impairment and legal blindness by cause and identify opportunities for case-control studies of disease etiology.

- Ocular Melanoma. In view of divergent opinions on the most appropriate means of treating this life-threatening disease, NEI plans a workshop in April to determine what the science base is and to identify future research initiatives.

- International Prevention of Blindness. This has been identified as an international health initiative by the President and the Department. The Institute has assumed a catalytic role in stimulating research in conjunction with the World Health Organization and is funding a three-year contract with WHO at an estimated annual cost of $150 thousand to support epidemiologic components of WHO's Programme for the Prevention of Blindness. Among the research needs in this area are efforts to apply existing technology, epidemiological research, and basic research on the adaptation of current techniques to the special needs of developing nations.

Civil Rights and Affirmative Action Initiatives

An agreement has been reached recently between NEI and NIA to share the services of an EEO coordinator. This is a positive step. The Institute also has an EEO Committee and an EEO Counselor.

Chapter 10

NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES

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Chapter 10

NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES

Director's Preface

The budget of NIGMS is devoted almost exclusively to the extramural support of research and research training at universities, medical schools and similar institutions throughout the country. The research and training supported by NIGMS undergird the research areas of all the other, categorical Institutes.

Since the major part of this research is basic and undifferentiated, priority is based primarily on opportunities for major advances in knowledge in a given program area and on the probability that new findings will ultimately contribute to the prevention, diagnosis or treatment of disease.

It is characteristic of the basic research projects supported by the Institute that they evolve and change character, often in an applied direction, when circumstances and opportunities warrant it. As this happens, the investigator's activities may become more appropriately supported by one of the categorical Institutes and the grant is transferred accordingly. In other words, there is a continuing turnover of grants supported by NIGMS such that new ideas and new investigators can be tested constantly and given a chance to contribute to biomedical knowledge. In the aggregate, the Institute's grantees constitute a vital national resource that continually generates new ideas and knowledge. But this resource must be maintained and carefully nurtured, and, while the Institute is always alert to new opportunities and initiatives, it also recognizes a responsibility to minimize the impact of budgetary instability and rapid policy changes on already ongoing projects. Changes of commitments and directions on short notice lower the productivity of research laboratories. A vital factor in optimizing available grant resources is a staff of health scientist administrators who are knowledgeable about the most recent advances in their respective areas of scientific expertise.

Consistent with its mission to support basic, undifferentiated research, the Institute's programs of applied and clinical research are relatively small. However, in trauma and burn research and anesthesiology, the Institute will continue to give special emphasis to relevant physiologic investigations. A knowledge of the key physiologic functions in these patients cannot prevent trauma, but should allow more effective intervention and prevention of post-traumatic complications. A better understanding of the clinical pharmacology of anesthetics is essential in order to increase the safety and efficacy of anesthesia. From the physician's vantage point, trauma, burns, and use of anesthesia are not preventable, but their adverse medical consequences can surely be minimized to the benefit of both the patient and his pocketbook.

The Institute's role in research on genetic diseases is focused on the underlying, general and fundamental concepts that apply to genetics in general

and to whole groups of genetic diseases, while research centered on a particular genetic disease is usually supported by one of the other Institutes, depending on its major characteristics. Occasionally, a particular genetic disease may be studied by an NIGMS grantee, particularly within one of the genetic research center grants, in which case it serves as a model for understanding other diseases as well.

It is our conviction that the ultimate result of the basic, laboratory-oriented research supported by NIGMS will be the prevention of much illness whose nature we now do not understand. At this stage, however, we have no way of knowing which illnesses will be preventable. It depends almost entirely on unforeseeable laboratory advances which have no definable correlation with monetary expenditures for specific projects. On a large scale, of course, there is a correlation between budgets and results, provided the scientific opportunities exist. It is in the grant applicant's professional self-interest to seek out the most promising of these opportunities. We also have evidence that our grantees have strong human incentives to have their work not only widely communicated, but also applied toward improved health care.

FY 1981 Program Changes

Major Activities to be Maintained in FY 1981

Research on Membranes

Continued emphasis will be given to exploitation of recent advances in our understanding of the structure and function of cell membranes. These include the following: (1) the discovery of specific "receptors" on neurons for a growing number of transmitters, including oligopeptides; (2) the discovery that cells have specialized receptors which recognize specific circulating enzymes and participate in their uptake--this has important implications for replacement therapy of various genetic diseases caused by the lack of particular enzymes; (3) indications that the number of insulin receptors is related to the concentration of insulin in the plasma--this has great significance with regard to our understanding of the control of insulin and blood glucose levels in the body; and (4) indications that other blood constituents, such as lipoproteins, also seem to have specific "target" cells.

Further research advances in this area could hold the key to major breakthroughs in the prevention, diagnosis, and treatment of various genetic, endocrine, cardiovascular, neoplastic, immunologic, and neurologic diseases, and, due to a number of recent technical advances in the identification and isolation of membrane components, increased opportunities for progress are now at hand.

Polygenic Disease

While many of the common genetic diseases due to a single gene alteration have now been described, there remains a major group of diseases in which genes play a significant role but are not the sole determinants of disease. These so-called polygenic diseases, which include hypertension, atherosclerosis, diabetes, cancer, and schizophrenia, are believed to result from a combination of genetic and environmental factors. The study of the genetics

of such diseases is therefore much more complex. However, new concepts have evolved and progress is being made in the identification of specific genetic factors which contribute to these diseases. The results of these studies are being used both to identify persons at high risk for the diseases and to modify environmental or genetic factors when this is possible. We expect significant progress in this area in the next few years.

Genetic Expression

Progress in the analysis of eukaryotic chromosome structure is offering clues to how the genetic information encoded in the nucleus of each cell in the body is expressed, and especially how that expression may be regulated. The fact that cells are different in major characteristics, while possessing the same genetic information, poses a major problem in biology whose solution will probably have relevance not only to our understanding of human development, but also of (1) aging, (2) neoplasia, (3) activation of latent virus, (4) triggering of "genetic" disease, and (5) the effects of drugs. There are hints that the kind of recognition or molecular matching exemplified by the antigenantibody reaction will turn out to be a model for understanding other subcellular processes, including genetic expression.

Research Instrumentation

Discovery of this increasing degree of structural detail is only possible through continuing advances in the development and use of analytical instruments and methodology. The Institute provides significant grant support in this area. However, the cost of these instruments on the commercial market is escalating, and access to them is becoming a problem. In conjunction with other components of NIH and the National Science Foundation, the Institute is searching for a practical way to support continued development and availability of these resources. In FY 1979, the Institute funded 65 grants specifically for the purchase of research analytical instruments to be shared among grantees of NIGMS as well as of other components of NIH. This was a one-time initiative which the Institute does not now plan to repeat (14 of the applications remaining in the backlog were funded in FY 1980). Anecdotal evidence points to a continuing need, but an administratively sound and more regular mechanism must be found to meet this need.

Trauma and Burn Research

Over the last few years, Institute grantees have made substantial progress in establishing the fluid and nutritional requirements of trauma and burn patients, and many of the advances have recently been published in a widely distributed manual. Further improvements are needed, however; this necessitates basic studies, at the cellular and molecular level, of the profound biochemical systemic changes that follow severe trauma and burns. In order to further encourage research on these problems, the Institute has announced in the NIH Guide for Grants and Contracts its continuing strong interest in trauma and burn research, and the availability of support for new investigators and for research training of future investigators in this area.

Research Training

Because much of the projected research, for the long term, will require scientists with a broad, multidisciplinary background (a category in short

supply), the Institute intends to continue to support research training in cell and molecular biology, genetics, pharmacology, and systems and integrative biology at selected, outstanding institutions for highly qualified and motivated candidates.

The emphasis in the faculty fellowship and visiting scientist portions of the MARC (Minority Access to Research Careers) Program will be on strengthening the research capabilities of the biomedical science faculty at minority institutions by expanding their contacts with majority institutions and promoting exchanges of not only personnel, but ideas and administrative "know-how" as well. The recently begun (1977) Honors Undergraduate Research Training Program at minority institutions has within it a feature that will be developed further--summer courses, or as much as a semester spent on studies and work away from the parent institution. These courses and laboratory experiences will be provided primarily by majority institutions, or specialized facilities, such as the Oak Ridge National Laboratory. An evaluation of the program, undertaken late in FY 1979, will have an impact on the subsequent level of support for this program.

Major Activities to be Cut Back, Eliminated, or Not Started in FY 1981

Drug Receptors

A highly promising area of research is the characterization of receptors for drugs and neurotransmitters in the intact organism or in the human. Many diseases and some types of drug resistance are now thought to be due to defective receptors as expressed through decreased affinity for substrates or decreased numbers. In addition, many drugs have now been shown to be effective because of their affinities for specific receptors; knowledge of these receptors' properties may make possible design of more specific and effective drugs. While isolation and identification of these receptors has progressed rapidly employing biochemical isolation techniques, only very recently have productive methods begun to be applied to the whole animal or to human investigation.

Systems Physiology

Both the maintenance of the "milieu interieur" and adaptation to the environment require coordinated control and regulation of a multitude of biologic functions. The techniques of control theory and systems analysis as developed by engineering scientists are expected to be promising tools for analyzing the roles of, for instance, various hormones and components of the nervous system in the regulation of composite biologic functions. This so-called "physiological control systems research" is still in its infancy, but it promises to become most productive and to be applicable in numerous medical areas. Among these are not only those primarily involving the nervous and endocrine systems, but all general, systemic disease, including the adjustment to trauma.

Metal Ions and Regulation

Metals have been known for some time as essential constituents of cellular enzymes and other macromolecules, but their exact functional role is

generally not well understood. Similarly essential to vital functions are certain relatively small metal ions, such as sodium and potassium, although their precise role remains largely unknown.

Calcium, having properties in common with both of these groups, is emerging as a particularly important element central to intracellular regulation of energy metabolism and cellular contractility. The major determining factor in the action of calcium seems to be the local concentration of the free ionized form, which results from interconversion with protein-bound calcium or other forms of "storage," on the one hand, and transport across the plasma or intracellular membranes, on the other. The detailed analysis of the mechanisms involved in these processes is attracting much attention from scientists, and such research promises to yield results of high relevance to a host of pathologic conditions.

The methodology and instrumentation used in these studies spans a wide spectrum, including work on isolated living or artificial membrane preparations, the use of special probes for measuring intracellular concentrations of calcium, and electron microscopy.

In addition to delaying these specific thrusts, there will of necessity be an across-the-board reduction in the award of grants to new investigators.

Congressional Directives Having an Impact on FY 1981 Plans

Trauma and Burn Research

In the Senate Appropriations Report for FY 1980, Congress has reiterated its strong interest in an expanded effort to support trauma and burn research. The Institute is trying to attract and encourage a greater number of grant applicants by announcing its continued strong interest in this area and the availability of a range of grant mechanisms for this purpose. Although there should be no doubt of the Institute's strong commitment, there appears to exist a shortage of well-trained and appropriately motivated scientists. For this reason, special attention will be paid to the research training programs which have served effectively as recruiting mechanisms in the past. There is some concern that the payback provision of the current law could be having a negative effect on recruitment.

Research Training

The Institute is continuing its emphasis on multidisciplinary predoctoral research training in order to help ensure that future investigators and NIH grantees will have received optimal preparation for productive research careers. Being preeminent at NIH in support of this type of training, the NIGMS feels a special obligation to stabilize and protect this activity. Within the rubric of research training fall two special programs, the Medical Scientist and Minority Access to Research Careers (MARC) Programs. The former addresses the serious problem that the number of research physicians has decreased substantially in recent years. Training of investigators who will have both a medical background and solid competence to do research in the laboratory thus

is of utmost importance. The National Academy of Sciences (NAS) recently recommended that this program be increased to support a total of about 725 trainees. Within the constraints of funding only the highest quality applications, the NIGMS is trying to reach this goal. The MARC Program initiated an Honors Undergraduate Program in FY 1977. To date, 22 awards have been made; further growth will be dependent upon staff evaluation of trainee selection and program effectiveness.

FY 1982 Program Changes

In light of the FY 1981 budget process, the following initiatives proposed for FY 1981 will be postponed to FY 1982: research on (1) drug receptors; (2) metal ions and regulation; and (3) physiologic control systems.

Continued cutbacks are planned in the following research programs: diagnostic radiology, anesthesiology, and automation of the clinical laboratory.

Diagnostic Radiology

Support for both research and research training within this discipline was given a strong impetus in 1966 with the Heart, Cancer and Stroke initiatives, and the Institute undertook activities which were not solely within the missions of one of the other Institutes. As a result of this stimulation, research support was increased significantly for a growing number of investigators. By its nature, the discipline touches many categorical interests at NIH, as each investigator has tended to focus on particular disease or organ problems, assigned generally to Institutes other than NIGMS, particularly to the National Cancer Institute and the National Heart, Lung, and Blood Institute. Recognizing this gradual change, the Institute has determined that decreasing resources should be allotted to this area.

Anesthesiology

To a somewhat lesser extent, a similar situation exists for anesthesiology. In this case, however, we would judge the stimulatory effort to have been less successful, and research in anesthesiology or pain research in this country cannot be said to be flourishing. Also, unlike the case with diagnostic radiology, a major biologic problem underlies research in anesthesiology--namely, elucidation of the basic mechanism of pain; this has proven remarkably resistant to research efforts. As a problem, it overlaps the interests of the National Institute of Mental Health, the National Institute of Neurological and Communicative Disorders and Stroke, and, indirectly, the National Institute of Dental Research. The decrease in research in anesthesiology relates to the severe lack, currently, of well-trained, interested investigators who can truly advance our knowledge. The first priority has to be research training of future clinical and basic scientists with an interest in anesthesiology, and the Institute is making great efforts to facilitate such training. These efforts have been further extended by the new program of special research grants for new investigators in anesthesiology, to help them make the transition from training to research.

Automation of the Clinical Laboratory

This program was also begun in 1966 as a result of the Heart, Cancer and Stroke initiative. It was recognized then that the steadily increasing demand for a wide variety of laboratory tests on patients could only be met by at least partial automation of tests performed in these laboratories. This, however, has turned out to be a two-edged sword in that it made possible and, indeed, facilitated the introduction and demand for additional tests. This increase was of course also stimulated by advances in medicine, such as a better understanding of hormone action, intermediary metabolism and electrolyte balance. Some of these tests, however, offer what is best described as "halfway" information in the context of their current use, since they represent second- or third-order measures of the relevant basic biologic function. Further, automation in the clinical laboratory without more than matching advances in our understanding of normal and pathologic processes would result in an undesirable imbalance, with adverse cost/benefit implications. Consequently, the Institute is currently deemphasizing this section of its overall program in favor of more basic studies of the cellular, molecular, and genetic bases of disease.

Following a recent review and evaluation of the Institute's Physiology and Biomedical Engineering Program, the Institute expects to reorient its support of biomathematics and statistics in order to stress projects that have a clear relation to biology. Conversely, projects concerned primarily with the mathematical aspects will be cut back.

NIGMS Stabilization Plan

Since the idea of stabilization implies that NIH would move toward a more constant competitive climate for the scientific community, such a constancy, or conservatism, needs to be maintained for each of the scientific disciplines, as reflected in the programs of the Institute operating branches. The NIGMS would therefore plan to maintain the relative allocations of resources to its four research programs. However, the Research Plan does envision a tilting toward the more basic and biologic programs (Cellular and Molecular Biology, Genetics, and Pharmacological Sciences), and giving particular attention to research on basic mechanisms involved in the Trauma and Burn area. There would be a gradual deemphasis of the development of methods and instruments, *per se*. Under a growing budget, the impact of this plan would not require a decrease in the absolute number of grantees in the Physiology and Biomedical Engineering Program. Considering both its mission and the expected scientific opportunities against a background of limited resources, the Institute plan is to emphasize investigator-initiated projects that would increase the science base.

Summary of NIGMS' Research Plan Review Session with the Director, NIH

The discussion was greatly enriched by the participation of Drs. Palade and Gottschalk, NAGMS Council members, Dr. Bennis of the NIH Director's Advisory Committee (DAC), and Dr. Thier, consultant to the DAC. Dr. Palade's suggestion that NIH support the development of standardized reagents, which are not commercially available and for which sufficient monetary inducement for production by non-Federal sources does not exist, is an intriguing one. Consideration of this type of proposal, which is predicated on effecting economies and improved quality through collective approaches, should be facilitated by the newly established Office of Research Services.

Program Overview

The discussion of the Institute's unique mission, program structure, and funding patterns indicated the following:

- As the Institute charged with the support of basic, undifferentiated research which undergirds the research areas of the categorical Institutes, NIGMS plays a pivotal role in stabilizing support for the basic biomedical sciences. The major portion of NIGMS extramural funds for research and research training are approximately equally divided between medical school departments and basic science departments in other academic institutions.

- NIGMS devotes a relatively small proportion of its budget to applied and clinical research. The Institute's involvement in many of these areas derives from the NIGMS mandate to support research areas or disciplines which transcend the interest of one or more of the Institutes. Conversely, when studies supported by NIGMS develop categorical relevance, they are transferred to the appropriate B/I/D. The NIGMS has documented well over one hundred cases where this has happened in recent years.

- The Pharmacology Research Associate Training (PRAT) Program is the Institute's only intramural activity. Currently, the program supports 22 Fellows performing pharmacological research under the guidance of preceptors in NIH and ADAMHA laboratories. A sub-program has been established under which a couple of PRAT positions are specifically targeted for clinical pharmacology in order to attract more physicians into this shortage area.

- With the exception of the Minority Access to Research Careers (MARC) Program, which is exclusively devoted to research training, the full array of support mechanisms is used in each of the other four major program areas. Approximately 74% of the current NIGMS budget is allocated to research project grants, and investigator-initiated research is accorded the highest Institute priority. Within the present funding climate, NIGMS is attempting to maintain a relatively constant level of support for its specialized research centers with a projected 30 research center grants to be funded in FY 1980. However, at the time of

recompetition, existing awards will be carefully evaluated, and the Institute's centers policy limits awards to $500,000 (direct costs) per year.

- The former Pharmacology-Toxicology Program has been renamed the Pharmacological Sciences Program to more accurately reflect its orientation towards basic studies to elucidate underlying mechanisms of drug action and to avoid the confusion that has resulted from the association of toxicology research with the environmental toxicology research supported by NIEHS.

Training

- The major proportion of the first group of NIGMS training awards made under the National Research Service Act will be eligible for renewal in 1980. As a result of the substantial number of new awards in FY 1980, the NIGMS training commitment base for FY 1981 is high; $54.4 million has been budgeted for non-competing training awards in FY 1981.

- NIGMS supports two-thirds of the trainees receiving predoctoral support from NIH through institutional awards. Since the advent of the NRSA, the Institute no longer awards individual fellowships for predoctoral study except under the Minority Access to Research Careers (MARC) Program. It was also noted that the number of predoctoral trainees supported has declined since the implementation of the NRSA.

- Postdoctoral support is provided through both individual fellowships and institutional awards. Individual fellowship applications are no longer reviewed by the NAGMS Council; however, Council is kept apprised of this activity. As a result, the Institute has been able to shorten the period from receipt of application to the time of award to six months.

- NIGMS support for the MARC Program totaled $2.8 million in FY 1979 and is estimated at $3.6 million in FY 1980. The Program is designed to increase the number of minority scientists in biomedical research and to help strengthen the research and teaching capabilities of minority institutions. Three forms of support are encompassed under this Program: the MARC Faculty Fellowship Awards, Visiting Scientist Awards, and the MARC Honors Undergraduate Research Training program, the newest and largest component. Currently, 22 minority institutions are participating in the latter program and are receiving support for teaching and providing research training to honors undergraduates who are now in their third or fourth year of college and who plan to obtain the doctorate degree in biomedical science areas.

- NIGMS is presently supporting about 650 students at 23 institutions under the Medical Scientist Training Program which leads to a combined M.D.-Ph.D. degree. The Institute's annual investment in this Program, which is designed to increase the number of physician researchers, is about $7.7 million. NIGMS is attempting to meet the goal of 725 trainees, recommended by the Committee on Research Manpower Needs of the National Academy of Sciences, while continuing to fund only the highest quality applications.

Stabilization of the Science Base

The NIGMS supports the concept of stability and endorses efforts to introduce greater predictability into research funding patterns. The NIGMS approach to stabilization is predicated on the view that the commitment base should not be eroded to free up monies to fund new and competing awards. Several factors were cited in support of the NIGMS position that type 5 noncompeting continuation grants not be negotiated downwards, including (a) initial review groups are already being extremely restrictive in the evaluation of grant budgets; (b) the research that would be adversely affected is of excellent quality and, in fact, a substantial number of requests for supplemental funding to meet rising costs are being received from current grantees; (c) such a move would lend credence to the view now held in some quarters that there is flexibility in grantee budgets; and (d) a funding strategy under which commitments would not be honored is essentially disruptive to the research community.

Shared Instrumentation Awards

In FY 1979, NIGMS initiated a special one-time competitive grant program to provide funds for the purchase of research instrumentation to be used on a shared basis. The program was instituted to respond to perceived needs of NIGMS grantees for better access to modern instrumentation and as a means to promote sharing of equipment and dissemination of new instrumental techniques. The need for the program was demonstrated by the fact that 212 applications were received despite a period of only two months between the announcement of the program and the receipt date for applications.

The awards made ranged between $38 and $172 thousand and provide funds for expenses related directly to the purchase or upgrading of equipment. Maintenance costs and support for technical assistance may be provided to a maximum of $15 thousand per year for up to three years. The awards were made for a single analytical instrument or instrument system--most frequently equipment for nuclear magnetic resonance, electron microscopy, spectroscopy, protein sequencing, amino acid analysis, X-ray and computer graphics, and cell sorting.

NIGMS is to be commended for taking action to address an area of continuing need and for the efficiency with which this initiative was carried out. The Institute's experience with this program should prove valuable as we begin to examine collectively institutional needs in the coming year.

Research Emphases

The NIGMS research plan reflects a continued emphasis on the basic science areas within the Institute's purview. Continued cutbacks are planned in three areas: (1) diagnostic radiology where the research emphasis has shifted to categorical areas; (2) anesthesiology where the Institute is reorienting its efforts to move the field ahead by placing first priority on research training; and (3) automation of the clinical laboratory which is being deemphasized in favor of more basic studies. The Institute's Advisory Council has shared in these judgments.

Burn and Trauma Research

Since the NIGMS burn and trauma program was established in 1966, the Institute has sponsored research on the total systemic response of the body to trauma and burn injury that has produced an array of effective modes of therapy. However, continued progress in this area has been hampered by a lack of highly trained investigators. Therefore, NIGMS has initiated a number of actions designed to recruit more physicians into burn and trauma research.

NIGMS support for burn and trauma research is estimated at $12 million in FY 1980, an increase of 18% over FY 1979 expenditures. Approximately one-third of the total FY 1980 budget for this program has been allocated for 11 burn and trauma research center grants. The NIGMS emphasis of this area is consistent with the Senate Appropriations Committee's interest in an expanded research effort.

Civil Rights and Affirmative Action Initiatives

The actions taken over the past year in the areas of recruitment, career advancement, and training which are designed to improve the opportunities for minorities and women within the Institute are encouraging. An increment of $750 thousand has been allocated to the MARC Program in FY 1980 above the FY 1979 funding level.

Chapter 11

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

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Chapter 11

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

Director's Preface

The National Heart, Lung, and Blood Institute has been issued the mandate to marshall the Nation's health resources into a comprehensive National Program to prevent and treat cardiovascular, pulmonary, and blood diseases and to improve utilization of our national blood resources. The challenge of this responsibility is great. For more than 50 years, heart and blood vessel diseases have been the major cause of death in this country. Over the years, the programs of the Insitute have evolved as a coordinated effort to combat the devastating consequences of these diseases in terms of lowering morbidity and mortality and associated economic costs.

Magnitude of the Problem

Diseases of the heart, lung, and blood account for an inordinately large share of the sickness, death, and financial loss caused by illness, and the magnitude of NHLBI's responsibilities must be viewed in light of this burden. In 1978, of the ten leading causes of death in the United States, four fell within the purview of the NHLBI; diseases of the heart (first); cerebrovascular diseases (third); chronic obstructive lung diseases (sixth); and arteriosclerosis (eighth). These four major disease categories accounted for one million deaths, well over half of the total deaths in 1978.

Despite striking improvements over the last 20 years, diseases of the heart, blood vessels, lungs, and blood remain among the Nation's most serious health problems. Cardiovascular diseases constitute the leading cause of death for men over age 40 and for women beginning at age 60; and at least 40 million Americans have diseases of the heart and blood vessels. In addition, cardiovascular diseases caused 51.9 percent of all deaths in 1977. Heart disease, in particular, often causes long periods of limited activity and accounts for more bed days than any other condition. The economic burden of cardiovascular disorders is estimated to be in excess of $50 billion dollars annually, accounting for over 36 percent of all years lost to illness in 1974.

The social and economic burden of diseases of the lungs and respiratory system is equally severe. While these diseases cause fewer deaths than cardiovascular diseases, they kill earlier in life and account for more than five percent of all the potential years-of-life lost as a result of illness. In 1975, treatment costs for lung and related diseases amounted to $7.5 billion. Since blood diseases so frequently strike during childhood, standard economic measures cannot fully reflect the loss or costs in terms of suffering and grief. These diseases, including the hemoglobinopathies, are the cause or complication of a variety of serious disorders.

Research Program Strategy

The National Program Plan addresses specific scientific goals and individual program areas. In order to meet these goals, the Institute utilizes a program strategy that lends direction and momentum to the National Program as a whole. The program strategy employed for each of the disease-related mandates of the NHLBI consists of an ordered sequence: acquisition of new knowledge, testing and evaluation of promising hypotheses, and dissemination of new and existing knowledge.

Research Program Goals

Each of the three categorical Divisions has certain responsibilities and objectives in common with the others: increasing knowledge of normal and diseased organ systems through broad programs of basic and clinical research, clinical evaluation of research findings, and expediting the transfer of validated findings into medical practice; emphasizing programs of prevention; planning and coordinating research grant, contract, and training programs; evaluating existing activities and assessing future needs; and stimulating the health care communities to respond to identified needs.

FY 1981 Program Changes

Major Activities to be Initiated

No major activities will be initiated in FY 1981.

Major Activities to be Maintained

Heart and Vascular Diseases

Arteriosclerosis--Fundamental research on the etiology of arteriosclerosis; the biology of blood vessels; regression and development of arteriosclerotic lesions; new risk factors; primary prevention trials; lipid research clinics; research in basic, clinical and population aspects of arteriosclerosis; development and testing of non-invasive methods of detection and monitoring of atherosclerosis.

Hypertension--Fundamental research in inhibitors to kinins, kallikreins, and prostaglandins to more fully understand the physiological actions of these hormones; fundamental investigations toward improved diagnosis, treatment, and prevention of hypertension; a broadly focused hypertension education program directed toward the general and medical public.

Cerebrovascular Disease--Intensive study of the etiology and pathogenesis of cerebrovascular disease; development of animal models.

Coronary Heart Disease--Studies to limit the myocardial damage due to coronary events; development and testing of new techniques of emergency cardiovascular diagnosis and therapy; investigation of the mechanisms and factors which precipitate acute coronary events; major clinical trials

including Beta-Blocker Heart Attack Trial (BHAT), Aspirin Myocardial Infarction Study (AMIS), Coronary Artery Surgery Study (CASS), and a coordinated attack on the assessment and management of coronary heart disease.

Peripheral Vascular Disease--Studies to improve the diagnosis, therapy, and rehabilitation of peripheral arterial, venous, and lymphatic diseases; studies of the natural history of occlusive venous disease with and without surgery; studies of the effectiveness of various therapeutic procedures and drugs; noninvasive techniques for diagnosis and monitoring.

Arrhythmias--Investigation toward fundamental understanding and prevention of arrhythmias; studies of sudden death; and improvement of methods used to prevent, diagnose, and manage arrhythmias and other electrical disturbances of the heart.

Heart Failure and Shock--Laboratory and clinical studies that focus on the cellular factors leading to death of heart muscle; efforts to quantify the extent of heart muscle inadequately perfused or irreversibly damaged following a heart attack. (This includes the Multicenter Investigation of Limitation of Infarct Size (MILIS).)

Congenital and Rheumatic Heart Disease--Studies on the etiology of congenital heart disease; research on animal models; study of the immunological problems in heart disease and their management, specifically in relation to rheumatic heart disease.

Cardiomyopathies and Infections of the Heart--Experimental work to study the etiology and treatment of these diseases; investigation of a hereditary model of a form of cardiomyopathy.

Circulatory Assistance--Research, development and evaluation of short and extended term implantable heart devices and power sources; clinical evaluation of temporary left ventricular assist devices directed at the short-term management of heart failure and shock; research and testing development and evaluation of non-invasive methods of diagnosis and monitoring.

Lung Diseases

Structure and Function of the Lung--Studies of the ultrastructural and biochemical characteristics of individual lung cells and tissues; studies of the mechanisms of lung tissue damage and repair; studies of intermediary metabolism of lung; studies of basic lung physiology, the role of chemical, mechanical, and neural mechanisms in the control of ventilation, and the processes of gas exchange in the immature and mature lung in health and disease.

Chronic Obstructive Lung Diseases--Longitudinal studies of the natural history of chronic bronchitis and emphysema; studies to correlate biochemical and physiological alterations in early stages of chronic obstructive lung diseases; clinical trials to study the efficacy of nocturnal oxygen therapy in chronic obstructive lung disease and the use of intermittent positive pressure breathing for treatment of chronic obstructive lung disease.

Pediatric Pulmonary Diseases--Investigations to characterize the clinical, pathological, physiologic, biochemical, and molecular events associated with normal lung development, and the onset and course of hyaline membrane disease; clinical trials of the efficacy of antenatal administration of steroids in prevention of hyaline membrane disease.

Fibrotic and Immunologic Interstitial Lung Diseases--Investigations of specific agents responsible for fibrotic lung diseases in occupational environments, with specific attention to dose-response relationships; investigations relative to the immunological and biochemical responses to organic and inorganic dusts that lead to fibrotic lung diseases and hypersensitivity pneumonitis.

Respiratory Failures--Studies to elucidate the basic mechanisms of the adult respiratory distress syndrome; studies to determine how degenerative changes in the lung can be arrested or reversed.

Pulmonary Vascular Diseases--Development of non-invasive techniques for early detection and continuous monitoring of pulmonary hypertension and pulmonary edema; investigation of the structural, biochemical, and physiologic characteristics of pulmonary vascular smooth muscle.

Blood Diseases and Blood Resources

Red Blood Cell/Bleeding and Clotting Disorders--Investigations of the structure and function of protein coagulation and anticoagulation factors and elements; further elucidation of the mechanisms of action of prostaglandins and thromboxanes on platelet function; a search for drugs which affect platelet action and inhibit thrombosis; studies of the molecular and clinical aspects of thalassemia, especially the use of iron chelating agents; purification of erythropoietin through application of modern techniques; studies of the chemistry and function of the red blood cell membrane; a broad range of basic, applied, and clinical research directed toward increasing our understanding of the thrombotic process and improving our ability to prevent and treat thrombotic disorders.

Sickle Cell Disease--Development of techniques for studying the mechanism governing the switch from fetal to adult hemoglobin production; molecular studies aimed at the delineation of regulation of globin gene expression in general as well as the gamma and beta loci, specifically; studies on the metabolism of sickled cells; determination of the pathophysiology of sickle cell disease, with emphasis on the role of coagulation in vaso-occlusive crises; collaborative studies of the clinical course of sickle cell disease; activities in education, diagnostic, and counseling services.

Blood Resources--Develop and improve procedures for the acquisition, processing, storage, distribution, and clinical use of blood and blood products; conduct animal testing of new and improved fluorocarbon compounds for use as artificial blood substitutes; development and testing of oxygen-binding chelates in animals with more of their blood replaced by free-hemoglobin; studies on the collection, function, and transfusion of platelets and granulocytes; development of new methods of plasma fractionation; a study on "Blood Utilization", in order to encourage the use of blood components or plasma fractions instead of whole blood.

Major Activities To Be Cut Back, Eliminated or Not Started

The following major activities are planned to be cut back, eliminated, or not started in FY 1981:

- Investigator-Initiated Research: Over the past 10 years, the percentage of approved grant applications has declined steadily from 90 percent in the 1960's to a present level of 24 percent. At the 1981 budget level, the Institute expects to fund less than 24 percent of its competing (new and renewal) investigator-initiated research grant program; therefore worthy research proposals cannot be funded.

- Manpower and Training: Severe manpower shortages exist and continue to grow in the area of heart and vascular disease. Fewer and fewer new clinical trainees are entering the research fields. Present estimates show that physician trainees are entering these fields at a rate of approximately one-third of that of 1972. The FY 1981 level will not allow new training grant awards. The FY 1981 budget level will need to be augmented substantially to slow or reverse these trends. Furthermore, new and innovative manpower development programs, needed to fill gap areas and develop physician researchers and educators, will not be continued; new Preventive Cardiology Academic Awards and Clinical Investigator Awards will not be funded at the FY 1981 level.

- Application and Transfer Activities: For the second year, there will be no new initiatives and no needed expansion of ongoing activities in the clinical trial, education and demonstration areas.

Directives Resulting from FY 1980 Appropriations Committee Reports and Their Impact Upon FY 1981 Plans

- Cooley's Anemia: "The NHLBI should undertake an education program for patients and their families, the population at risk, and physicians regarding Cooley's Anemia." The Institute is developing an educational handbook on Cooley's Anemia and will expand its existing education program in this area for FY 1981.

- Hypertension: "The Committee will be looking forward to a report by the Director at next year's hearings as to what additional resources will be placed in this program during 1980..." The Institute is currently assessing all aspects of its multifaceted Hypertension Program. In addition, the Institute is cooperating with a committee of experts charged with reviewing the Program. The results of these assessments will be presented by the Director at the 1981 Appropriation Hearings.

FY 1982 Program Changes

Major Program Changes Planned for 1982

The following program changes presented below are in order of priority:

- Investigator-Initiated Research: A substantial increase in funding for investigator-initiated research will be required. This increase should allow the Institute to return in its grant funding rate to approach the 250 payline.

- Manpower Development: Increased support will be required in order to both maintain existing manpower levels in research fields directly related to heart, lung and blood diseases as well as sustain and further develop new initiatives to support investigators in specialized areas of major program interest.

- Training: Major support is essential to reverse the steady decline in the number of postdoctoral preclinical and clinical investigators in all areas of heart, lung, and blood research. Furthermore, additional resources are needed to sustain and further develop minority training programs.

The following program initiatives are planned for 1982:

Division of Heart and Vascular Diseases

The Role of Salt and Water in the Pathogenesis of Hypertension--Encourage and support research that will increase our understanding of the basic mechanisms whereby excess sodium intake participates in elevation of blood pressure.

Blood Platelets and Atherosclerosis--Study of the functional and structural effects of dietary modification on platelet-arterial wall interaction. The role of arterial wall prostacycline and platelet thromboxane and their inhibitors will be actively explored.

Community Surveillance System for Cardiovascular and Other Chronic Diseases--Establish a surveillance system to monitor, in 10 geographically circumscribed communities representing regionally different parts of the United States, possible concurrent trends in the incidence of first and recurrent myocardial infarctions, and cardiac deaths over time.

Longitudinal Studies of Coronary Heart Disease Risk Factors in the Young--Measure changes in risk factors (e.g., blood lipids and lipoproteins, blood pressure, adiposity, blood sugar) that have been associated with the development of coronary heart disease in cohorts of males and females from newborn to 30 years of age.

Clinical Trial of Hypertension in the Aging--A clinical trial, to be launched jointly with NIA, to determine the effectiveness of treating systolic hypertension commonly found in older persons. The potential impact from such a trial is now considered to be of major significance.

Cardiovascular Disease (CVD) Nutrition Research Unit for the Study of Nutrition and Heart and Vascular Disease--Establish close interaction and collaboration between investigators in CVD and nutrition, and offer a broad range of research training activities oriented toward human nutrition in health and disease.

Migration and Culture Change in Relation to Coronary Heart Disease--Research to study coronary heart disease morbidity and mortality in population groups that currently are undergoing rapid social change.

Studies on Efficacy of Combinations of Biobehavioral and Pharmacologic Treatments of Essential Hypertension--Promote and encourage clinical research projects dealing with evaluation of combinations of pharmacologic and non-pharmacologic therapies in the treatment of patients with diagnosed essential hypertension.

Behavioral Studies of Prevention Techniques--Build our understanding of methods of changing risk-prone cardiovascular disease behavior from the nutritional and behavioral data base developed through the Institute's clinical trials.

Studies on the Influence of Psychosocial Stressors in Smoking Cessation and Maintenance of Cessation--Obtain data to clarify the role of psychosocial stressors in smoking recidivism.

Small Blood Vessel Prosthesis--Conduct a program for the research, development, and evaluation of small vessel prostheses for use in pediatric patients with congenital heart disease and adult populations with peripheral vascular or coronary artery disease.

Animal Models for Study of the Pathogenesis of Cardiomyopathies--Study several models of cardiomyopathy in experimental animals and to evaluate the pathogenetic mechanisms of these conditions.

Expansion of Specialized Centers of Research in Arteriosclerosis--Continue study of hyperlipidemia and vascular diseases, including animal and tissue studies and basic laboratory investigations in eight centers.

Smoking and Heart Disease--Research to learn more bout the mechanisms by which smoking influences the development, pathogenesis, and manifestations of cardiovascular disease.

Feasibility of the Development of Markers to be Used as Adherence Measures in Clinical Trials of Pharmacologic Agents--Develop safe, stable and non-interfering, non-radioactive substances which can be added to pharmacologic agents which may be used in clinical drug trials or therapeutic intervention trials to assess patient adherence to the drug regimen.

Targeted Smoking Cessation for Cardiovascular High Risk Groups--Develop targeted smoking cessation programs specifically for populations of smokers who are at special risk for cardiovascular disease as a result of the combination of smoking and other exacerbating risk factors.

Division of Lung Diseases

Immune Complexes in the Pathogenesis of Pulmonary Fibrosis--Encourage studies on the formation and significance of antigen-antibody complexes in interstitial pulmonary disease in order to determine whether immune complexes represent an initiation, an unimportant consequence, or a contributing factor in chronic pulmonary injury in man and experimental animals.

Vascular Basement Membranes in Interstitial and Vascular Diseases of the Lung--Research to determine the structural and functional properties of the vascular basement membrane in interstitial and vascular lung diseases.

Expansion of Specialized Centers of Research in Fibrotic and Immunologic Diseases, Cystic Fibrosis, Chronic Obstructive Lung Diseases, and Pediatric Pulmonary Diseases--Conduct basic, applied, and clinical research projects for chronic airways, pediatric pulmonary, fibrotic and immunologic pulmonary and pulmonary vascular diseases in the 19 specialized Centers.

Prevention of Pulmonary Emphysema in Patients with Alpha-1-Anti-Trypsin Deficiency--Develop and test synthetic low molecular weight elastase inhibitors for the treatment of patients with the genetic deficiency of alpha-1 antitrypsin.

Cell-to-Cell Interaction in the Developing Lung--Conduct fundamental studies to define the interactions between lung cells in developing lungs; determine the contribution of interstitial cells to lung development.

Studies of Neuro-Histopathologic Changes in Obstructive Airways Diseases--Support fundamental studies directed at elucidating the morphologic features of the sensory and motor innervation of the airways during development, health, and disease and at correlating the morphological information with their physiologic function.

Immune Responses in the Lung--Encourage research to define immune responses within the lung; to identify agents known to produce lung disease, particularly fibrotic and/or granulomatous lung disease.

Characterization of Periciliary Fluid in Mammalian Airways--Isolate and characterize the aqueous environment (periciliary fluid) between the mucus and epithelial surface and to establish how this fluid influences the mucociliary clearance process in health and disease.

Division of Blood Diseases and Blood Resources

Modified Hemoglobin--Test various forms of modified hemoglobin as blood replacement preparations.

Factor VIII Preparation--Research to improve methods of harvesting, preparation and eventual use of Factor VIII. Particular emphasis would be on the development of methods to ensure that the cryoprecipitate produced by hospital and community blood centers would not be wasted.

Dietary Lipids and Hemostatis--Investigate the role of dietary lipids in hemostatis and thrombosis with regard to platelet lipids, and to determine if there are any changes in the functional activity of platelets.

Donor-Recipient Compatibility in Platelet Transfusion Therapy--Research to determine which patterns of platelet transfusions are most clinically beneficial and most cost-effective, to assure optimal transfusion therapy for patients requiring long-term platelet support.

Deep Vein Thrombosis--Conduct a cooperative study of laboratory methods for determining patients at high risk to deep vein thrombosis.

Leukophoresis Donor Safety Study--Conduct a multifaceted study of the effect of leukopheresis on repeat donors to develop guidelines that assure donor safety and assist in donor selection and care. These data are necessary as a prelude to licensure for the product.

Sterile Connecting Device for Blood Bags--Demonstrate and evaluate the most promising existing types of docking devices in terms of potential uses, acceptability to the user communities, cost-effectiveness, and safety and efficacy.

Cardiac Function in Sickle Cell Disease--Evaluate cardiac function and the nature, prevalence, and incidence of cardiac impairment in patients with sickle cell disease as a special study within the Cooperative Investigation of the Clinical Course of Sickle Cell Disease.

Summary of NHLBI's Research Plan Review Session with the Director, NIH

Program Overview

The major focus of NHLBI is on basic biomedical research, although legislative changes over the last decade have expanded the Institute's mission. In 1969, the Institute added lung diseases to its mission and was designated as the National Heart and Lung Institute. The National Heart, Blood Vessel, Lung, and Blood Act of 1972 increased the Institute's mandate to include research on blood diseases and the management of our Nation's blood resources with the Institute assuming its current name in June, 1976. In addition, this legislation specified percentages of funds to be allocated among the three program areas of heart, lung, and blood and added the requirement for the Institute to conduct dissemination and translation activities. To accomplish this expanded mission, the NHLBI has developed a very extensive and iterative implementation planning process which sets research priorities over a fourteen-month planning cycle. Priorities for uncommitted FY 1980 funds are:

- new institutional and individual research fellowship grants,
- new and competing research project grants, and
- new initiatives and other program expansions.

Stabilization of the Science Base

The NIH proposal to stabilize the science base in general and research project grants in particular, the manner in which the NHLBI would implement such a proposal, and the potential impact stabilization could have on the full range of Institute activities was discussed. It was agreed that scientific opportunity is an essential criterion for establishing needs in the science base, but it is also essential to try to provide some level of predictable funding of this major activity to the biomedical research community. The concerns of the Institute are not incompatible with stabilization, and as this concept is refined and extended to other components of the science base, much progress will be made in dealing with the problems which remain.

Within a level budget in 1982, the NHLBI would propose to approach stabilization of the science base by funding the same number of competing research project grants as in 1981 (but below its FY 1977-1979 average of 810 grants per year), increasing funding for research centers, intramural research and direct operations by 8% to offset inflation, and absorbing reductions in training, research career programs, and research and development contracts. Within a constrained budget, these funding patterns would obtain through the 1984 planning period, except that substantially fewer and fewer competing research projects would be awarded and research and development contracts would be reduced significantly. Most of the Institute's application and transfer activities would be slowed down. If additional, modest resources were made available in 1982, these latter activities would be restored to previous levels.

Priority Scores

For 1980, priority score projections were based on the funding convention of each Institute for research project grants. Of the two priority score methods traditionally used, "raw" or "normalized," NHLBI based its funding decision on "normalized" priority scores. Institutes using a "normalized" system of scoring required less funds to reach the payline of 212 determined by the House Appropriations Committee than if they had used the "raw" priority score convention for their projections. In 1981, all Institutes will be using "raw" priority scores, which are now termed "actual" scores, for their projections.

Training/Manpower Development

As a result of the decision to put all funds above the commitment base into competing research project grants, NHLBI will not fund any new training awards in FY 1981.

The current situation vis a vis clinical training in the three program areas of heart, lung, and blood is varied. There is a need for academic cardiologists, as the majority of those trained in cardiology are going into practice. The specialty of pulmonary medicine has emerged and flourished under the sponsorship of NHLBI. On the other hand, the specialty of hematology is undergoing change and is gravitating toward the more specialized area of hemato-oncology. There are, however, clear needs for researchers in the science and management of blood banking.

Clinical Trials

The Institute has identified new opportunities in the Applications category, if additional funds were available. For example, two clinical trials could begin immediately on systolic hypertension in the elderly and validation of non-invasive techniques for the assessment of large vessel atherosclerosis.

- One of the most important advances to date has been the results of the Hypertension Detection and Follow-up Program. The HDFP has recently terminated its clinical phase, yielding data demonstrating that treatment of mild hypertension increases the patient's lifespan. As a result of this trial, a new program will be undertaken in FY 1980 to track the progress of former HDFP patients as they re-enter the conventional medical care and treatment system.

- Results of AMIS, the five-year Aspirin Myocardial Infarction Study, will be published in February in the Journal of the American Medical Association. A news release is scheduled to coincide with JAMA publication.

Cardiovascular Epidemiology

The program includes studies on risk factors in the young that predispose them to hypertension, the association between stroke and heart disease, and reasons for the decline in the mortality rate for cardiovascular diseases. In

FY 1979, this program supported $5 million in grants and $2 million in contracts. Three major initiatives have been developed and will be implemented as funds become available. These initiatives, in order of priority, are:

1. Community surveillance systems for cardiovascular and other chronic diseases,

2. Coronary heart disease risk factors in the young, and

3. Migration and cultural change in relation to coronary heart disease.

Major Civil Rights and Affirmative Action Initiatives

A status report on NHLBI civil rights and affirmative action initiatives for FY 1979 notes:

- The Office of Special Concerns, OD, was established and a Federal Women's Program Coordinator appointed.

- The updated statistical profile of Institute staff distribution by race and sex indicates that women have increased in numbers and in grade level over the past year.

- Minority and female membership on all NHLBI chartered public advisory groups has increased.

- The Institute continued its cooperative minority programs with MBS and MARC and the Minority Hypertention Research Development Summer Program.

Research Advances

A number of recent research advances were highlighted, including new information gained in the following areas:

- Prostaglandins (endoperoxides)--The balance between thromboxane A_2 from blood platelets and prostacycline PGI_2 from vessel endothelium has been further elucidated; studies show that aspirin at low doses affects thromboxane but not prostacycline. Also, the lipid composition of platelets affects their production of thromboxane. Other studies indicate that abnormal levels of prostacycline and thromboxane occur in diabetes.

- In the prorenin $\rightarrow$ renin $\rightarrow$ angiotensin I $\rightarrow$ angiotensin II cascade this year it has been demonstrated that kallikrein catalyzes the conversion of prorenin to renin. In addition, a specific antagonist of the conversion of angiotensin I to angiotensin II has been synthesized and is now in Phase III trials. Captopril, an oligopeptide that can be taken orally, has been shown to have a low toxicity and considerable value for the control of high blood pressure.

- Plasma protease inhibitors--Amino acid sequence studies of antithrombin III, the first sequence of a plasma protease inhibitor, has shown that

it has no homology with other known antiproteases, e.g., trypsin inhibitors from plants, etc. Alpha$_1$ antitrypsin and antithrombin III, however, have been found to have sequencing identities.

- Clinical research highlights included the clinical use of noninvasive techniques to study serially left ventricular function post drug (e.g., adriamycin) and post surgery (e.g., coronary bypass) as well as increased interest in coronary vasospasm as a cause of angina, heart attack and heart death and vasodilator therapy in congestive heart failure and primary pulmonary fibrosis.

- The conclusions and findings of the HDFP are of major significance vis-a-vis the diagnosis and treatment of our nation's 40 million plus hypertensives.

Dr. Higgins and Dr. Willman, members of the National Heart, Lung and Blood Advisory Council, and Dr. Braunwald, a consultant to that group, participated in the review session. Their perspectives on the issues were extremely valuable to the discussion.

Chapter 12

NATIONAL INSTITUTE OF NEUROLOGICAL AND COMMUNICATIVE DISORDERS AND STROKE

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Chapter 12

NATIONAL INSTITUTE OF NEUROLOGICAL AND COMMUNICATIVE DISORDERS AND STROKE

Director's Preface

A base of information and technology is now available for an expanded national research effort on understanding how the nervous system functions and for developing improved methods for the prevention and therapy of the neurological and communicative disorders.

In order to provide for these opportunities, the Institute's primary objectives are to:

Research Grants

- maintain a base of one-third of research grant funds for competing research project grant (R01 and P01) applications;
- as a minimum target, fund one-half of all approved competing research grants;
- give special attention to selected areas of clinical research; and
- meet all grant commitments.

Training

- give emphasis to the recruitment and scientific preparation of a cadre of highly skilled young people to maintain the NINCDS research effort; and
- give special priority to the individual fellowship program; use institutional awards in selected areas of national shortage (e.g., clinical research, neuroimmunology).

Intramural

- compensate for the past decline in position slots necessary to maintain a program of scientific excellence;
- provide the additional funds required for "other objects" in order to provide for inflation costs; and
- establish the new PETT (positron emission transverse tomography) and neurotoxicology research programs.

Significance of the Health Problem

Great strides have been made in recent years in understanding the physiological processes of the nervous system including the processes of hearing and speaking. Yet, formidable problems remain. The presence of neurological illness or major communicative handicap in a family creates severe emotional, psychological, physical and financial stress. Since many of these diseases are protracted and debilitating, they drain family and national resources and exhaust the human spirit in countless ways. Nowhere is the burden of illness greater or the quality of life more significantly marred than in the chronic debilitating disorders of the nervous system. Current estimates indicate that more than 50 million patients are affected with these neurological and communicative disorders in the U.S. alone, and that the health care costs exceed $65 billion. The magnitude of societal cost and long-term suffering places a high priority upon neuroscience research nd constitutes one of the greatest challenges to improve the quality of life.

Research Program Strategy

For many of the neurological and communicative disorders the causes are still unknown, preventive measures do not exist, diagnostic procedures are often nonspecific, and treatment is either nonexistent or only partially effective. Much of the research is necessarily basic since the fundamental biochemical and pathophysiological processes underlying most of the neurological and communicative disorders are only beginning to be understood. Investigator-initiated research proposals (R01s and P01s) continue to be the major mechanism of Institute extramural research support.

At the interface of fundamental research and applications research there is continuous monitoring by the Institute of special needs which are not receiving adequate attention but which are, nonetheless, necessary bridges to clinical application. At the technology transfer front a focal point has been established in the Office of the Director to work closely with the NIH Office of Medical Applications for Research and to identify appropriate topics for state-of-the-art appraisal, consensus development and transfer to the medical community. A technical consensus on the therapy of febrile seizures is presently in the planning phase as is a cooperative consensus meeting with the NCI on CT scanning.

The Institute continues an active program in the area of information transfer. In collaboration with the National Library of Medicine (NLM), a number of computer programs have been written and distributed as a series of leaflets which, through the MEDLINE information retrieval system, provide access to approximately 600,000 references in the fundamental neurosciences covering the current year and the preceding two years. A similar effort in the area of the communicative sciences, also in collaboration with NLM, has resulted in the recent publication of a "MEDLINE Users Manual and the Thesaurus for Specialists in the Communicative Disorders."

In the area of training, an adequate cadre of specialized research manpower is essential for maintaining the viability of the neuroscience research enterprise. The need to maintain the training program is obvious so that young talented minds with both wisdom and skills are attracted and technically

prepared for careers in neuroscience research. Also, noted investigators from other disciplines, for example, genetics and molecular biology, must have the opportunity to pursue the exciting and challenging field of neurosciences.

The Intramural Research Program of NINCDS remains the nation's single most important source of new neuroscience information and scientific leadership. Yet, inflation and position cuts have seriously threatened the abilities to maintain a high level of scientific excellence. The Institute emphasizes the need for stable support to the intramural activities in terms of positions and purchasing power so that basic and clinically applied investigations keep pace with newly emerging opportunities.

Goals

During FY 1979, as a joint activity with its National Advisory Council, the Institute has developed a comprehensive long-term research strategy in collaboration with distinguished clinical investigators, basic scientists, and representatives of the concerned public. The strategy entitled "National Research Strategy for Neurological and Communicative Disorders" articulates 107 scientifically accepted goals for the Institute.

FY 1981 Program Changes

Major Activities to be Initiated in FY 1981

Because of the increased grants commitment as well as a significant increase in competing renewal applications expected in 1981, the Institute does not expect to be able to initiate any major new research grant or contract initiatives.

Major Initiatives to be Maintained in FY 1981

The Institute would sustain the present level of research activities in the areas of neurological disorders of early and adult life, MS, dementia, pain, convulsive disorders, demyelinating and neuromuscular disorders. New initiatives started in response to the recommendations of the Epilepsy and the Huntington's Disease Commissions and related Congressional directives would be continued, but at a reduced level.

Congressionally directed research on the evaluation of vestibular functioning and the etiology of serous otitis media would be continued. Recently initiated projects on the epidemiology of noise-induced hearing loss, the development of high frequency audiometry and improved hearing aids with signal processing capabilities would be maintained. Studies on development of stuttering in young children and speech production aids for non-vocal patients with Parkinson's disease, amyotrophic lateral sclerosis or multiple sclerosis would be sustained. The development of the X-ray microbeam speech movement tracking system initiated in FY 1980 would be continued in order to provide new knowledge on speech movement characteristics.

The Institute expects to continue its comprehensive centers in central nervous system (CNS) trauma and in stroke at about one-half the planned level

of support. Any further reduction would make future restoration of epidemiologic and technology transfer activities more costly than their maintenance. The support of Positron Emission Transverse Tomography (PETT) projects initiated in FY 1979 would be maintained in accordance with the five years support assured to the grantees to allow their efforts to come to fruition.

The support of fundamental neuroscience research would be maintained to continue the support for basic neurological research including developmental, adaptive and regeneration phenomena; the study of local neuron circuitry and central processing; the role of hypothalamus and neuroendocrine peptide hormones on brain and body function, including blood pressure; safe methods for chronic stimulation of neural tissue; the evaluation of presently available capacitor electrodes for use with neural prosthetic implants; and the study of the effects of cerebellar stimulation on animal models of movement disorders.

The Institute expects to maintain at a reduced level its activities in biometry and epidemiology in order to continue development of data banks to permit research in prognosis and natural history of stroke and traumatic coma, and to complete surveys in progress on the incidence and prevalence of selected major neurological disorders.

The Institute will make every attempt to maintain its Intramural Research Program, embracing important and unique aspects of basic and clinical neurosciences research. Studies of disorders, such as Parkinsonism, epilepsy, Huntington's chorea and muscular dystrophy, and of neurotransmitters which have yielded potent new drugs capable of alleviating the debilitating symptoms of Parkinsonism and related disorders, will continue.

Major Initiatives That Must be Cut Back, Eliminated or Not Started in FY 1981

The restraint of the FY 1981 budget will adversely affect the stability of the investigator-initiated research programs resulting in payment of less than one-third of the approved research grant applications in fundamental neurosciences. However, clinical research support will be endangered to even a greater extent because clinically-oriented research applications typically receive relatively poorer priority scores than basic science grant applications.

The Institute may be forced to curtail or postpone the following research efforts: (a) exploration of promising leads in lipid storage disease, Reye's Syndrome, autism, Alzheimer's disease, demyelinating and sclerosing disorders, and diabetic neuropathy; (b) implementation of some of the Commissions' recommendations (and Congressional directives) aimed at the control of Huntington's disease and of epilepsy, especially those of the Urban Comprehensive Epilepsy Center and the Huntington Disease Centers Without Walls; (c) determining individuals' susceptibility to noise induced hearing loss; (d) implementation of screening methods to provide early detection and treatment of laryngeal cancer, and epidemiological studies of the prevalence of speech and language disorders in children and the effects of treatment on their prevalence; (e) research contracts on studies of the control of the neurogenic bladder, electrochemical reactions associated with metal electrodes, and methods of increasing the rate of information transfer into sensory cortex; (f) support of Comprehensive CNS Trauma Centers which relate to research on the prevention of

paraplegia by therapeutic and rehabilitative modalities; (g) speed of data collection and analysis in the national controlled clinical trials of EC/IC anastomosis for the treatment of TIA, and in the study on the use of steroids in the treatment of spinal cord injury; (h) implementation of a new national targeted collaborative effort with NCI on CNS tumors, particularly primary tumors of brain; (i) planned completion of stroke and traumatic coma data banks aimed to improve patient care, and the redesign of hospital discharge forms for the National Hospital Survey of Diseases, which is a joint effort of several National Institutes of Health, the NCHS, the Bureau of Census, and the CDC; (j) intramural research initiatives emanating from Nobel Prize winning studies on the transmissibility of slow virus infections, defective virus particles, the body's autoimmune mechanism, together with the studies that require production of enzymes, antigens and reagents; (k) the proposed Intramural Communicative Disorders Clinic, and operation and staffing of cyclotron supported PETT facilities.

Directives Resulting from FY 1980 Appropriations Committee Reports and Their Impact Upon FY 1981 Plans

For 1980, NINCDS has received an increase over the 1979 budget. Congressional Committee directives have specified that this increase be used in emphasizing many of the areas of our ongoing research activities including understanding of the process of transduction in hearing, causes, prevention and treatment of hearing loss, research on spina bifida, autism, and Batten's disease. The Institute has been instructed to continue the implementation of the recommendations of the Commissions on Epilepsy and on Huntington's Disease. The Committees have also expressed strong interest in research on spinal cord regeneration and on diabetes. All these research efforts in 1980 are estimated to produce an increase in grant commitments in 1981.

FY 1982 Program Changes

Major Program Changes Planned for FY 1982

FY 1982 will be the third year for the implementation of the National Research Strategy for Neurological and Communicative Disorders. Its implementation, if supported by the budgetary process, requires a modest growth in the Institute's research budget until 1984 and subsequent stabilization through 1989.

This plan incorporates significant new initiatives with emphasis proposed in the following areas: (a) CNS plasticity, developmental neurobiology on cell proliferation and migration, dendritic development, synaptogenesis, cell susceptibility to insult; (b) pathophysiology and etiology of the most common disorders of the developing nervous system; (c) the nature, neural mechanisms, causes and remediation of chronic destructive pain of diverse origins and the neurochemistry of opioid peptides; (d) human communication and its disorders, including hearing, speech and language; (e) viral and infectious agents, including "slow" virus and unconventional virus agents and their possible link to etiology, and neurochemistry and pathophysiology of a range of degenerative chronic neurological disorders; e.g., Huntington's Chorea, Parkinson's disease, Amyotrophic Lateral Sclerosis, Alzheimer's disease; (f) immune factors

in neurological disease, endocrine and hormonal abnormalities, and other endogenously or possibly genetically caused disorders of the nervous and neuromuscular systems; (g) changes in CNS metabolism and biochemistry as a consequence of trauma and stroke and development of diagnostic and interventive techniques to avoid permanent tissue damage and aid restoration of function; (h) mechanisms of axonal transport and chemical factors influencing nerve growth and regeneration; (i) neuronal structure and function and potential prognosis for differing treatments through the use of PETT; (j) detection, diagnosis, and treatment of CNS neoplasms; and (k) neurophysiological and neurochemical correlates and bases of complex human behaviors including memory, appetite, emotion, language, and higher cognitive functions.

Potential Impact of Program Changes on Three Year Period (1982-1984)

In the communicative disorders area NINCDS expects to see increased sophistication in sensory aids for the deaf, improved understanding of the effects of noise on hearing, knowledge of the brain organization underlying language functions, methods for the early detection of speech misarticulation and stuttering in children, and the prevention of hearing loss resulting from otitis media in children.

The proposed budget for FY 1982 would allow further development of grant supported Comprehensive Stroke Centers by 1983, of Comprehensive CNS Trauma Centers by 1984, and of Comprehensive Coma Centers by 1985; thereafter, local resources would assume a major part or all of the funding responsibilities for the public information aspects of these centers. The grant-supported spinal cord regeneration research program would also continue its orderly growth. The PETT program would likewise be supported and its research applications explored and demonstrated.

The proposed budget would allow us to proceed with synthesis, animal screening, clinical testing and development of anti-epileptic drugs. The progress would continue to implement the recommendations of the Commissions on Epilepsy and on Huntington's Disease. Increased understanding is expected to be achieved in the events of neurobiological development, timing of insult in determining the nature of neuronal disruption, and the processes of demyelination and degeneration. Research in fundamental neurosciences will lead to an enhanced understanding of basic problems; e.g., how information is transferred between brain cells and stored, local neuronal interactions and the significance of brain asymmetry. It is expected that the recently developed knowledge relating to the understanding of the basic principles underlying neural prostheses will be increasingly utilized.

The establishment of a model intramural clinical research team with expertise in otolaryngology, audiology, and the speech and language sciences is planned on the NIH campus with the opening of the Ambulatory Care Research Facility. NINCDS is also planning a collaborative project with the Clinical Center, NIA and NIMH to install an intramural PETT facility equipped with a cyclotron.

Summary of NINCDS' Research Plan Review Session with the Director, NIH

Stabilization of the Science Base

The discussion of stabilizing NIH support of the science base, particularly as it would apply to predictable funding for research project grants, indicated that NINCDS would prefer to approach stabilization somewhat differently. Within a constrained budget the Institute would not necessarily choose to fund competing research project grants at the expense of support for other elements of the science base, such as the intramural research program. Commitments in all major categories of support would be maintained, resulting in a reduction in the overall rate of funding for competing research projects.

In FY 1981, the Institute would distribute any additional resources in the following order of priority:

- Training--Additional funds would be invested in individual training awards (F32s) to bring the number of training awards up to the FY 1980 level. The five major manpower studies conducted in recent years by the Institute would justify this increased support in the area of neuroscience training.

- Intramural programs--Additional money would provide needed budgetary relief for the intramural programs for programmatic increases and to keep up with inflation.

- Contracts and competing grants--The remainder of any budget increase would be divided between increases in the number of competing research project grants, research centers, research career programs, and increases for contracts for drug testing and development. Additional contract funds would provide for initiation of clinical trials on CT scanning, brain tumor treatment, brain trauma, and agents that affect the immune response.

Extramural Program Mechanism Conversions

In accordance with discussions at previous review sessions, NINCDS is proposing to convert the comprehensive centers now funded by contracts to the research centers mechanism and has also submitted a proposal to OD, NIH for the conversion of the clinical research centers to research project grants.

- Clinical research centers--These projects have been identified as P50 center grants, but as a result of last year's review session, it was apparent that they more closely resemble program projects (PO1s) and should be considered for reclassification into this category. NINCDS currently supports 59 of these "clinical program projects" for a total of $28.3 million.

- Comprehensive centers--Three of the five existing Comprehensive Epilepsy Centers are in the process of being reviewed for conversion from contracts to P50 center grants. These centers contain core support

with outreach activities and are initiated by contract. After a five-year development period, the intent of the Institute has been to convert the research aspects of these centers to the grant mechanism. One new comprehensive Epilepsy Center in an urban area is planned to be initiated by contract in FY 1980 in response to a recommendation by the Epilepsy Commission.

Intramural Program Issues

Concern was expressed by the Institute over the erosion of its intramural program due to several years of little or no growth. NINCDS feels that its intramural program represents an important scientific resource, and that intramural investigators should be considered equally with extramural investigators in defining the science base.

The intramural programs are going through a difficult transition phase; but these will be expected to share in austere budgets along with the extramural community. During this period, however, the intramural programs must not be allowed to deteriorate. Perhaps it will be necessary to consider new mechanisms for the distribution of human resources in order to preserve the intramural programs' record of excellence.

Training

Up to now, the Institute has favored the use of individual fellowship awards over the institutional training mechanism. Currently, over 50% of training awards made by NINCDS are to individuals. However, because of no new training awards in 1981, there will be a 27% reduction in individual fellowships between 1980 and 1982. This decline has led to a recommendation to the NINCDS Advisory Council for a shift in training priorities to increase the relative numbers of institutional awards supported by the Institute. This new position taken by the Institute will affect how NIH achieves the requirement for a 15% floor for individual training awards, as NINCDS has provided for a large portion of this total number in the past. With training consuming 5% of total NIH funds and the decline in training over the last 10 years, it is clear that such issues as this should be included in a much needed, overall NIH training strategy.

Major Civil Rights and Affirmative Action Initiatives

The NINCDS continues its participation in the MARC and MBS programs. For the 1979 summer program, the Institute exceeded the NIH goal for minority participation. Also, over the past year the Institute EEO office has expanded. In the coming year, a training seminar for supervisors and expanded efforts for increasing minorities and women in staff fellowship and associate positions and on advisory committees are planned. In addition, the Institute plans to increase its efforts in reaching the local Hispanic community.

Drs. Cooper and Plum, members of the National Advisory Neurological and Communicative Disorders and Stroke Council, participated in the review session. Their perspectives on the issues were extremely valuable to the discussion.

Chapter 13

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Chapter 13

DIVISION OF RESEARCH RESOURCES

Director's Preface

Resources funded by DRR are an essential part of the NIH science base, providing necessary facilities and capabilities for conducting research. Developing alternatives to such DRR resources through categorical channels would be more expensive and less effective. Efforts to stabilize the science base should address multicategorical research resources, which are developed and sustained by DRR and available to all investigators.

This plan focuses upon those areas which need particular attention so that the Division can provide facilities and capabilities to a wide range of investigators in an efficient, coordinated, and cost-effective manner.

In recent years, there has been a profound expansion in the number and capabilities of technologies, available from the physical sciences and mathematics and through advances in engineering, which can be brought to bear on biomedical problems. The Biotechnology Resources Program is committed to, and uniquely structured for, exploiting these technologies. This program has consistently distinguished itself by striving to make appropriate new technology available to the broadest range of investigators in the most effective, efficient, and responsive manner.

Fortunately, there is some reversal of the past rapid decline in purchasing power of this program which has severely limited investigators in more fully utilizing the latest technological advances. Actions proposed in 1981 and in this research plan will stem this decline and enhance the capabilities of this program to meet the needs and opportunities of this exciting area.

An unusually high rate of inflation in program costs has limited DRR's ability to support the best and most necessary General Clinical Research Centers. Further major decreases in the number of patient days being supported would seriously damage clinical research in this country at a time when the need for the application of results of basic research to human problems in becoming of increasing concern. Therefore, DRR will strive to remain near the current level of research-bed capacity.

Similarly, the Division's commitment to providing essential non-human primates for research will continue. The importance of this effort is continuously increasing as the sources from which primates have traditionally been obtained continue to be cut back or eliminated.

Another area requiring continued attention is Biomedical Research Support. The May, 1980, report of the National Commission on Research ("Funding Mechanism: Balancing Objectives and Resources in University Research") cites the Biomedical Research Support Program as the one successful model of the kind of program that, if the model is extended to other fields of research,

can prevent the otherwise inevitable deterioration of the productivity of the national research enterprise. The flexibility in scientific management which these funds give PHS grantee institutions will become even more crucial in the 1980s as the effects of overall economic restraints are felt. The level of funding for this program, in proportion to overall PHS research grant funding, should at least be maintained so it can continue to have meaningful use and impact. The method used to allocate these funds among grantees will be adjusted to heighten this impact upon the institutions most actively engaged in biomedical research.

There are, of course, other important research needs and opportunities worthy of attention. These have been set out in the DRR Five-Year Plan, and they will be addressed in turn in the research plans of future years. The focus for this specific research plan has been on those areas most needing attention no later than FY 1982.

FY 1981 Program Changes

In FY 1980, the Minority Biomedical Support Program will make a start in complying with Congressional instructions to expand activities to reach significant groups of minority students in institutions which have not previously received support from the program. In FY 1981, this initial level of activity will be maintained at the expense of other MBS program activities.

In FY 1980, the Biotechnology Resources Program will begin supporting resources in two new areas--simulation analysis and synchrotron radiation. Program funds will also be used in FY 1980 to strengthen resources that were underfunded in FY 1979. In FY 1981, the program's funding posture will be sufficiently flexible to allow funding of important new technologies and facilities as opportunities occur.

The Congressionally supported and directed major initiative in primate breeding will be maintained, although expansion of this effort will not be possible. A modest increase in resource-related research projects is expected in the Animal Resources Program. These projects, most of which will be concerned with infectious diseases of laboratory animals, have the potential for the greatest impact for the limited funds that can be made available. This increase will be made possible by an offsetting decrease in support of certain special animal colonies which are of lower Division program relevance.

The threshold for support by the Biomedical Research Support Program and the formula for allocating that support among the program's grantees, will be studied in FY 1980. In 1981, the results of this study will be used to change the program so that more of its funds will be awarded to the institutions most actively engaged in research.

The planned phase-down of the Biomedical Research Development Program, resulting from a decrease in the overall quality of the competitive pool, will continue. As planned, there will be a decline from 30 awards in FY 1980 to 19 in FY 1981 and the last ten in 1982. Funds made available will be returned to the formula allocation portion of the BRS Program.

Research patient days supported by the General Clinical Research Centers Program will decline slightly in FY 1981. Also, the initiative in clinical information-handling capability (the CLINFO system), will be cut back even further; only four will be distributed in 1980 and none in 1981.

FY 1982 Program Changes

Division program areas requiring priority support above the FY 1982 Current Services Level are in the following rank order: (1) the enlarging of existing, and establishment of new, unique shared Biotechnology Resources so that recent, new, and emerging technological advances can be made available to biomedical investigators, (2) the retention of the existing research-bed base of the GCRCs, and (3) the meeting of some of the previously identified primate breeding and supply goals.

Biotechnology Resources Program

Requirements and demands in the scientific community appear unabated for shared and special resources during the mid-1980s. Actions proposed by DRR for various resource areas are focused on opportunities to strengthen the science base and to bring greater shared resource systems, technologies, and expertise to the solutions of medical health problems through applications of fundamental science and technology.

Enlargement and Enrichment of Existing Base

Biomedical Structure and Function:

- The synchrotron radiation initiative of 1980 and 1981 will be expanded by the provision of additional resources to access this technology, one beginning in 1982 and one in 1984. The Department of Energy and the National Science Foundation have funded several projects to develop synchrotron radiation centers. Thus, national shared biotechnology resources cooperatively funded with the National Science Foundation and the Department of Energy will be needed to exploit this new radiation capability for biological and medical research.

- One high-resolution Nuclear Magnetic Resonance (NMR) resource for study of solids will be established in 1982, one in 1983, and one in 1984. High-resolution NMR is being usefully applied to the study of partially ordered biological structures which include cellular and organ membranes and collagen-rich tissues. Work in this broad field requires very high technology and expert technical support which have to be made more widely available through development of a resource which can be shared.

Biomedical Engineering:

- A new resource in implantable microsensor technology is planned for 1982. The new resource will engineer protective and bioinert materials to enclose the microsensors for implantation.

- Further development of a 1980 initiative will be to establish two simulation analysis resources in 1982 to provide increased capabilities to new areas of application for mathematical simulation and modeling techniques: circulatory mass transport, blood tissue exchanges, membrane exchange kinetics, and ionic membrane transport. Some more specific aspects of biomedical simulation analysis will be exchange of small solutes, water, ions, metabolic substrates and kinetics of exchange of large molecules, proteins, and lipoproteins.

New Initiative

- A new biomedical structure and function initiative will provide access to a specialized resource for acoustic imaging microscopy in 1982. In the early 1980s, NMR imaging and acoustic imaging, relatively new technologies, will be utilized to complement roentgenography and light microscopy as procedures for visually scanning the internal structures in the body. Acoustic imaging microscopy, an intensively developing technology, is anticipated to be ready for development as a resource in 1982.

General Clinical Research Centers Program

The level of funding requested for FY 1982 will enable the existing research bed base available to support clinical research to be retained. Increased effort is needed to sustain the national level of high-quality activity in this area because of disturbing declines observed in clinical research activities. General hospital wards cannot cope with the complex patient care and treatment required by clinical research. A special environment is needed. GCRCs provide about 75% of the federally supported clinical beds dedicated to research available in this country outside the NIH campus in Bethesda. Most inpatient research on conditions such as coronary disease and other cardiac disorders, hypertension, kidney disease, diabetes, and much of that on cancer is carried out in these centers. Investigators holding NIH research project grants or working on NIH center grants usually have adequate provisions for laboratory support for their human studies, but do not have funding for the patient-bed and clinical-care costs. The expenses for such studies cannot be borne by the subject of the investigation and will not be borne by hospitals or insurance carriers. As a result, investigators without access to facilities like those in the General Clinical Research Centers often cannot address the clinical application of their laboratory studies.

The extent to which the Centers increase the extension of NIH-funded research to direct studies on human-disease problems is illustrated by analysis of NIH support of investigators using Clinical Research Centers. Investigators utilizing the Clinical Research Centers in 1980 are expected to have between $250-300 million in support from other NIH grants and contracts, representing by far the largest proportion of NIH activity impacting on extramural research on human subjects. Over 90% of these investigators will be examining problems related to heart disease, hypertension, renal disease, diabetes, cancer, child health, and stroke. Fewer than 5% of these investigators will have hospitalization or patient care costs included in their NIH awards.

The days patients spend in these Centers are essential for advances in patient-oriented research. It is clear that the GCRCs provide the major means for carrying out the crucial human applications of those studies in which insights reached in basic research are translated to clinical situations. Maintenance of their function is essential for efforts to improve the health of our people and to apply the knowledge gained in basic research to the prevention, control, and alleviation of human illnesses.

Animal Resources Program

Primate breeding and supply will be a major focus of the Animal Resources Program. The breeding efforts at the Primate Research Centers need to be expanded to achieve near self-sufficiency within the mid-1980s. Although the Centers have increased their domestic breeding efforts rather significantly during recent years, their 1978 production of nearly 1,500 primate animals (all species) fell short of the 2,500 animals used that year. Conservation practices and improved breeding techniques need to be further developed, applied, and made known to the scientific community.

Funding for primate supply projects has been markedly increased over the past five years. This increase was provided to begin a program of domestic breeding to offset shortages of primates resulting from a drastic reduction in the number of non-human primates that could be obtained from natural sources. In fact, all species of primate animals are presently classified by the Convention on International Trade in Endangered Species as either clearly endangered or likely to become so.

The actions being considered in the area of primate breeding and supply include the establishment of an additional rhesus monkey breeding colony producing 700 animals annually; a contract producing an additional 600 cynomolgus monkeys annually; and solicitation of grant proposals for research on the nutrition, diseases, behavior, reproductive biology and production of selected species of primates. Also possible is a contract for breeding 25 chimpanzees a year and a project grant for research to establish the usefulness of the common marmoset for biomedical activities. Support will be continued for primate population field studies which contribute to the solution of primate supply problems and for the primate supply information clearinghouse.

In summary, the DRR has carefully selected from a wide range of needs and opportunities for research resources--of many types identified in the Divisional Five-Year Plan, 1982-86--those resource areas of highest priority in stabilizing and enhancing the NIH science base.

Summary of DRR's Research Plan Review Session with the Director, NIH

It is clear that as the NIH moves ahead in its efforts to stabilize the support of research project grants, we must also strive to better understand the environment within which research is conducted and the problems facing research intensive institutions. The programs of DRR provide a good focus through which we can gain a better view of the concerns to which we must be responsive in order to maintain our capacity to conduct biomedical research. I understand your view that a policy of stabilization, narrowly interpreted, could have a serious impact on DRR programs.

Please extend my thanks to your Advisory Council members, Drs. Benirschke, Johns, and Wilson, for their participation in the review session. Their insights from an institutional perspective contributed greatly to our discussion.

1981 Program Plans

The status of your 1981 plans based upon financial assumptions that at that time would have permitted a modest over-all increase in funding for the Divison were discussed, as follows:

- Clinical Resources

  (1) It is planned to stabilize these resources at approximately 175,000 research patient days per year (based on 80% occupancy rate) and 80,000 research outpatient visits. Five centers were phased out in 1979, and it may be necessary to phase out as many as four additional centers in 1981.

  (2) In order to maintain this bed capacity, additional funds for this program will be required. Options to combat rising costs through additional cost-sharing arrangements are becoming more restrictive.

  (3) The major allocation of patient days is currently in the area of endocrinology and metabolism, followed by clinical pharmacology and nutrition.

- Biotechnology Resources

  (1) There will be a modest shift in the allocation of dollars in this program area in 1981, with support to biological structure and function increasing about 8%, to biomedical engineering about 1% and support to computer technology resources decreasing by about 9%.

  (2) The above shift will result in approximately a 10% increase in nationally shared resources and about a 7% decrease in institutionally shared resources and a 3% decrease in resource-related project grants.

(3) No new awards are planned by NSF under their Regional Instrumentation Facilities Program until a detailed evaluation of current sites has been completed. This decision may result in a modest increase in the number of applications received by NIH in this area, but does not represent a major problem at this time.

- Animal Resources

(1) The dollar allocation in this program area will remain steady in 1981, with approximately 71% of the support going into primate resources and breeding and the remainder into other laboratory animal science activities.

(2) Even within this allocation, only 50% of the annual inflationary costs in the Primate Research Centers Program can be met. In addition, there is a pressing need for renovation of the physical facilities of all the primate centers, due to their age and heavy usage.

(3) Primate breeding requirements are accounting for an increasing share of dollars. If DRR is to attain its goal as recommended in the National Primate Plan, additional funds will be necessary in 1982 and future years.

- Minority Biomedical Support

(1) In 1980, some modest expansion of activities to reach groups of minority students in majority institutions will occur. This level of activity will be maintained in 1981, although at the expense of other program activities.

(2) This program has cooperative agreements with nearly all the Institutes. The Institutes are expected to establish a close working relationship with the grantees in order to develop categorically oriented research at MBS supported institutions.

1982 Priorities

The four major goals that the Division has set forth for 1982 were discussed. The comprehensive and thoughtful planning process that the Division has gone through in establishing these goals is impressive. They are:

- Enlarge existing and establish new shared biotechnology resources
The following technologies should be ready for development as a resource soon, and the Division plans to provide some support in these areas:

(1) Synchrotron radiation--This technology with its unique properties, especially in the very high intensity X-ray region is excellent for some biological applications such as low angle X-ray scattering. Both the NSF and the Department of Energy are becoming involved in

the development of this technology, and possible opportunities to develop National resources cooperatively funded with these agencies will be explored.

(2) Simulation analysis--This technology can provide the capability to analyze data from biological systems using mathematical simulation and modeling techniques. New areas of application could be circulatory mass transport, blood tissue exchanges, membrane exchange kinetics, and ionic membrane transport.

(3) Acoustic imaging microscopy--Low resolution images of tissues and organs can now be prepared using acoustic radiation. Resolution and techniques are expected to improve to the point of broad application in the next several years.

Expanded support is planned in the following areas:

(1) Microcomputer science and technology--This technology is becoming as powerful and capable as minicomputers and with considerable savings in cost and space. Recent developments are headed towards lightweight, low cost battery powered portable systems. These systems will greatly increase computer usage in laboratory and field applications.

(2) Micro-sensor technology--Efforts underway in the resources already in this area have provided new and useful devices for measuring and monitoring physical and chemical reactions occuring in the body. An additional resource-related research project will be for the development of a fuel cell that derives its power from the chemical energy in the body. This device, when coupled to a pacemaker, could eventually be devised to last throughout the lifetime of the recipient user.

(3) High resolution NMR--High resolution NMR of solids was recently developed and has excellent potential for biomedical work. Partially ordered biological structures, such as membranes and collagen-rich tissues, are being usefully studied by these methods. This area requires a very high technology and expertise and is ready for development as a resource. This area may be a good candidate for development as a regional resource.

- Strengthen the Biomedical Research Support Program--You expressed concern that the percentage relationship of BRS funds to research grant funds has been declining and believe that the program should be stabilized at an appropriate level. The Division is currently studying possible changes in the eligibility thresholds and allocation formula for awards in this program. The formula used to compute the amount of BRSG awards has resulted in a major change in the distribution of funds with smaller institutions receiving a larger portion of the funds awarded each year. This change has resulted in a situation which must now be corrected by revising the formula in order to provide a greater proportion of funds to those institutions most actively engaged in research. It will also be necessary to reassess the eligibility requirements to ensure that BRSG awards continue to be made to institutions that have

sufficient health research to justify an award. In addition to obtaining the advice of the General Research Support Review Committee and the National Advisory Research Resources Council with respect to proposed changes, it is also important to hear from the institutions themselves in terms of potential impact resulting from changes.

It is my understanding that the phase-out of the Biomedical Research Development Grant Program is proceeding smoothly, and any funds formerly provided for these awards will be allocated to the BRSG program.

- Retain existing base of clinical resources--Stabilizing the number of research patient days per year at 175,000 and research outpatient visits at 80,000 are the most critical elements to retaining the existing base of clinical resources supported by the Division. To do this will require some additional funding.

  In addition, greater emphasis will be placed on the Clinical Associate Physician (CAP) Program. This program provides opportunities to young physicians to develop into independent clinical investigators and adds to the professional resources of the General Clinical Research Centers where these individuals carry out their work.

- Meet primate breeding, research and supply goals--The estimated annual requirement for nonhuman primates for NIH extramural programs including the Primate Research Centers is 11,280 animals. The proportionate share DRR has of the National Primate Plan breeding goal is 6,255 animals. Programs currently underway will have an estimated production of 3,400 animals in FY 1980, or about 54% of the goal. The cost of this production will be about $2.5 million in 1980. For the Division to meet 100% of its breeding goal, additional funds will be required in 1982. It is extremely important that an adequate number of primates are bred domestically. Current primate shortages are impeding research in a number of areas.

Chapter 14

JOHN E. FOGARTY INTERNATIONAL CENTER

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Chapter 14

FOGARTY INTERNATIONAL CENTER

Director's Preface

Mission

In June 1979 a Task Force established by the Director, NIH, ended its year-long assessment of the missions and functions of the Center. Their report emphasized that the Center is an integral part of the NIH and urged that the relationshp be maintained and strengthened in order to provide a strong central focus for the international aspects of the NIH's biomedical and behavioral research.

Current Status

NIH has initiated a nation-wide search for a new director of the Fogarty Center. Until he or she is selected and installed, it would be premature to decide on details of long-range programs. However, it is possible at present to discuss the Task Force recommendations and to describe the development of a structure for their implementation. During the last year, a reallocation of support personnel has been made and the FIC intends to hold several positions vacant for use by the new Director in setting up new programs.

General Recommendations of the Task Force

The Task Force made three recommendations directed toward strengthening the overall organization, leadership and management of the Center: (1) establish an Advisory Board for the Center, (2) give the Director of the Center the additional title of Associate Director for International Activities, NIH, in recognition of the increased role of the Center as the central focus at NIH for international activities; and (3) select and develop new personnel at the Center. All three recommendations have been partially implemented.

In consonance with the Administration's desire to keep the number of public advisory bodies to an absolute minimum, the Director, NIH, has asked seven Institute Directors to act as ad hoc advisors to the Center. The group is expected to provide advice on ways to stimulate and strengthen the Center's scientific programs, to fulfill its coordinating and support functions and to achieve close and effective working relationships with the Institutes. At some appropriate time it may be possible to establish a more broadly based Council, as suggested by the Task Force.

Analysis of Programs in Relation to the Task Force Recommendations

The Center's present major programs as well as those envisioned by the Task Force, can be grouped into three distinct areas. One area--advanced studies--is explicitly stated in the full name of the Center and is listed

first in the mission statement. Over the years, however, it has not developed as a fully recognized major program. There have been many valuable scholarly works produced by the Center, and the Scholars Program brings outstanding scientists to the NIH campus each year, but there has never developed within the Center a focus for such activities. A restructuring of the advanced study program is needed for it to reach its true potential; a proposal that it be patterned after the intramural programs of the Institutes has been approved in concept by the Director, NIH.

Making up the second major area are the fellowship, grant, and contract programs that account for a large portion of the Center's appropriation and primarily support activities outside the Center. These are clearly analogous to the extramural programs funded by the Institutes, which also account for the bulk of their expenditures. The third area has no direct analog in the Institutes--the important role of the Center in the coordination of all international programs of NIH. This includes direct program responsibilities; coordination with the Office of International Health (OIH) and other agencies; staff assistance to the Director, NIH; hospitality for foreign visitors; and the administration of the International Visiting Program.

Each of these areas is discussed at more length below:

Advanced Studies Program

At present the advanced studies of the Center reside almost entirely in the Fogarty Scholars' activities. The Scholars Program has been a great success in bringing to the campus outstanding leaders in many areas of biomedical research. Selection as a Fogarty Scholar is highly esteemed, and the Center has achieved a world-wide reputation for this prestigious program. The Task Force questioned whether Scholars devote their time and attention to a single or very limited number of laboratories during their stay here; they implied that the program may be only a "distinguished visiting scientist" program. In some instances this is undoubtedly true, but in the vast majority of cases in recent years the Scholars have taken the initiative in organizing seminar series and major conferences on important topics of NIH-wide interest, and they have interacted with each other and with intramural scientists throughout the campus. We believe, however, that these interactions can be increased by providing additional opportunities to the Scholars, such as regularly scheduled seminars and luncheon meetings; by planning with each Scholar well in advance of his arrival the overall goals of his or her stay; by planning in advance for resource material that will be needed; and by better scheduling of Scholars so that synergistic effects may be obtained through the simultaneous presence of two or more Scholars in similar or complementary fields. Other changes in the program suggested by the Task Force are being studied.

Policy Studies Program

As the highest priority recommendation, the Task Force recommended that "there by established within the FIC a Policy Studies Program to address issues and topics concerning the international aspects of biomedical and behavioral research, research manpower training, and the transfer of research results to health care systems." The Task Force believed that the Policy Studies Program should include provision for:

1. A small core of FIC staff analysts to conduct, manage, and participate in policy studies;

2. A process to attract mid-career and junior scholars to the program;

3. The participation of Fogarty Scholars-in-Resident where appropriate;

4. A mechanism to support studies by skilled analysts; and

5. The conduct of conferences, workshops, and symposia growing from and in direct support of ongoing policy studies.

The FIC agrees that the development of a Policy Studies Program should indeed be accorded high priority. In view of the major impact that the proposed program will undoubtedly have on the character and future direction of the Center, definitive actions to initiate the policy studies programs have been deferred for consideration by the permanent Director. Over the past several months, however, the FIC has formulated a conceptual framework within which such a program might be developed.

To reflect and encompass the broad array of studies that could conceivably be undertaken, it has been suggested that the program be named the International Issues Study Program. The salient features of this program would include:

- An "intramural" program comprised of a small permanent staff of analysts (a "scientific director" and three or four professionals).

- Additional junior, mid-level, and senior analysts--recruited for limited periods of time as staff fellows or as appointees through the Intergovernmental Personnel Act--to augment and complement the efforts of the permanent staff by planning and conducting independent studies or by participating in joint efforts with the core staff.

It is anticipated that the program will be modified and refined as experience is gained from initial studies.

In line with the recommendations of the Task Force, we believe that the Scholars-in-Residence will serve as an extremely valuable resource for the policy studies program. A modest expansion of the Scholars program will be needed to insure the necessary breadth of interest and expertise without impinging on the present successful efforts to attract Scholars whose interests are closer to those of the Institutes' intramural programs.

The overall the Advanced Studies Program consisting of the Scholars-in-Residence Program and the International Issues Study Program, can become a dynamic and valuable adjunct to the present NIH intramural research efforts. Together they provide the means for the NIH to reach out beyond the borders of current research programs to explore international aspects of many scientific areas. The scholarly works produced in such a program should be of value not only as a resource to the NIH but in many instances to other agencies of the Public Health Service, as well.

International Cooperation and Coordination

The Center provides policy guidance, coordination and general oversight for the participation of NIH, together with other U.S. agencies, in bilateral cooperative agreements between the U.S. Government and a number of other countries. These include the People's Republic of China, Egypt, France, the Federal Republic of Germany, Hungary, India, Israel, Italy, Japan, Poland, Romania, the Soviet Union, Spain, and Yugoslavia.

The Task Force Report reinforced the importance of this part of the Center's mission and made recommendations designed to enhance the role of the Center as an integrating focus within the NIH for international activities. The Center should: (1) increase the professional staff available to support the coordination function; (2) establish an NIH-wide committee to exchange information, discuss the implementation of policies, and promote a greater international community of interest at NIH: and (3) establish and maintain a resource readily available to the Director, NIH, which would provide a comprehensive assessment of the status of and plans for NIH international activities. Other recommendations are aimed at establishing and maintaining closer relationships with the Office of International Health, the World Health Organization, and the Pan American Health Organization.

During FY 1980, the Center began to implement essentially all of these recommendations. For example, one professional and a research assistant were recruited for a one year period to assist in the development of a computerized base of information on Chinese scientists and research institutions. It is anticipated that this data base will form a framework for a system which will provide a continuing source of information on biomedical research in China.

Emphasis will be placed on the continued development of ways and means to ensure the NIH-wide coordination of international activities and on the improvement of intergovernmental relations with the People's Republic of China, Japan, Eastern European countries, Latin America, and the Middle East.

International Visitors Center

The International Visitors Center provides a point of reception and information for foreign visitors to the NIH campus; arranges visits of official international scientific groups and delegations; and handles the administration of the intramural Visiting Program. As the Visiting Program has expanded during the last few years, the administrative workload has increased substantially. In addition, the Visitors Center has expanded the range of services provided to newly arrived scientists in the Visiting Program.

In the interest of facilitating communication between the staff of the Visiting Program and the staff of the Institutes, the Task Force recommended that the FIC develop a handbook that describes in detail the duties and responsibilities of both the Institutes and the FIC regarding the administrative management of the visitors programs."

In January, 1980, the FIC published and distributed a "Handbook for the NIH Visiting Program Participants" to advise participants of important facts

concerning the visiting Program, and to describe life at NIH and living conditions in the Metropolitan area. This publication has been a "best seller" and will be entering a second printing.

The FIC is developing a companion handbook intended for the NIH sponsors of participants in the Visiting Program. This publication will describe in detail the steps that a sponsor must take in requesting an appointment for a scientist in the Visiting Program.

Fellowships

The Center funds and administers two major fellowship programs: (1) the International Research Fellowship Program which provides fellowships to foreign scientists at the postdoctoral level to enable them to pursue research studies in laboratories in the United States, and (2) the Senior International Fellowship Program, which awards fellowships to mid-career faculty members of U.S. universities to study abroad and to share their expertise with host institutions. In conjunction with the Senior International Fellowship Program, the Center administers a Special Emphasis Fellowship Program in aging, arthritis, diabetes, tropical diseases, and epilepsy in cooperation with the appropriate NIH institutes. The Center also provides administrative and review support to NIAID and NINCDS for the WHO-Institute collaborative fellowship programs in tropical diseases and the neurosciences. In addition, the Center processes applications for fellowships offered to young American postdoctoral scientists by the Swedish Medical Research Council, the Swiss National Science Foundation, and the French National Institute of Health and Medical Research.

The Task Force had three recommendations concerning this program: (1) design and implement a tracking system for follow-up data on former fellows; (2) consider expanding the age and experience criteria for the IRFP: and (3) consider directing special attention to the research manpower needs of the less developed countries. The Task Force also encouraged the development of further special emphasis fellowship programs with other Institutes of the NIH. These recommdnations are being reviewed by the Center's staff. In response to the first recommendation, a computer-based information system has been developed which contains pertinent data on each of the fellows who participated in the International Research Fellowship Program during its 20-year history. Using this data base, in conjunction with the MEDLAR system, the FIC has completed an initial evaluation of the International Research Fellowship Program. The results of this study will be available soon. This data bank forms the foundation of a "tracking system" which, through continuous updating and refinement, holds promise of providing a reliable mechanism for facilitating the conduct of a variety of analytic studies to assess the effectiveness of the Fellowship programs.

In the past the Senior International Fellowship applications were reviewed initially by the Division of Research Grants, while the others were given primary review within the Center. Henceforth, all types of applications will be submitted to DRG to insure uniform, high quality review commensurate with other grants and fellowships. Final review and award will continue to be handled through the Center.

Conferences

Scientific meetings play a major role in the exchange of information among research scientists. The Center, in addition to providing direct financial support of meetings, collaborates with NIH Institutes and other Federal agencies in the joint sponsorship of a wide range of scientific meetings supported exclusively through contracts. The Center serves as a "broker" in arranging for joint sponsorship of conferences, provides a share of the joint funding, supplies logistical support, directs editorial and publicaton services, and assists in the distribution of reports from the meetings.

Because of concerns about the quality of the review process and the appropriateness of generalized conference support in light of the Center's international mission, the Task Force recommended that the Center withdraw from the general support of conferences and focus its activities on the initiation, planning, and conduct of meetings on topics directly related to international aspects of biomedical and behavioral research, especially in relation to the new Policy Studies Program.

The Task Force felt that conferences should be supported through the traditional conference grant (R13) mechanism, with multiple assignment by DRG of applications in basic science areas that cut across Institute lines. In November, 1979, the Acting Director of FIC established a FIC Task Group on Conference Support to consider the recommendation of the Task Force and to suggest ways in which it might be implemented without creating a disruptive effect on the scientific community. The report of the Task Group, delivered in March, 1980, reaffirmed the view expressed by the Task Force concerning the support of conferences in general and the role of FIC in particular. The Task Group noted, however, that a need may continue for a "broker" to facilitate the award and funding of conference grants that are of interest to several Institutes. The Task Group suggested that the role might be played by DRG, NLM, or a lead-Institute but stopped short of recommending a particular site or organizational arrangement to serve this need. The FIC is currently reviewing the report of the Task Group as a point of departure for a staff effort, in cooperation with the candidate organizations, to determine a workable arrangement for the transfer of this function.

PL-480 Grants

The Special Foreign Currency Program provides grants for research in several countries where the U.S. owns "excess" foreign currency. As these funds become depleted in given country, this type of grant is being phased out. Ongoing grants are currently supported in Tunisia, India, Poland, Egypt, and Pakistan while new projects are being started in only the last four of these countries. Some State Department "special" funds provide support for a limited number of projects in Yugoslavia. As recommended by the Task Force, the Center is developing projections for the future of PL-480 grants in individual countries and will explore alternative mechanisms for support in order to minimize the effect created by the loss of these funds to investigators, especially those in developing countries.

Summary of FIC's Research Plan Review Session with the Director, NIH

The mission of the Fogarty International Center (FIC) has been the subject of discussion and study over the past several years. Those deliberations culminated in the study by the Task Force to Assess the Mission and Functions of the Fogarty International Center which was established to review the existing programs of the FIC and make recommendations for strengthening its role as the central integrating focus for NIH activities related to the international aspects of biomedical and behavioral research.

The report of the Task Force contains many thoughtful recommendations for modifying and expanding the functions of the FIC. The FIC, in return, has devoted considerable attention to examining the ways in which those recommendations might be best implemented.

The Acting Director of the FIC faces a difficult task in attempting to formulate plans for implementing the recommendations while at the same time reserving for the future FIC Director the freedom to make policy choices in shaping the nature and character of the Center. Delays in the appointment of a new full-time Director of the FIC place inordinate demands upon the Acting Director and senior staff of the FIC. Everything possible will be done to expedite the process of selecting the new Director. In recognition of the increased role of the FIC as the central focus at NIH for international activities, the Director of FIC will be given the additional title of Associate Director for International Activities, NIH.

Fellowship Programs

The FIC will attempt to stabilize the International Fellowship Program beginning in FY 1982 by awarding new fellowships annually to young foreign postdoctoral scientists to study at U.S. institutions.

In FY 1979 the program supported a total of 130 fellows. In FY 1980 and FY 1981 the number of fellows supported will decline to approximately 106 for each of those years. In FY 1982 the goal of the FIC is to restore the program to its 1979 level of 130 fellows.

The Senior International Fellowship Program, initiated in 1974 to permit outstanding mid-career faculty members of U.S. universities to study abroad and share their expertise with foreign host institutions, has proved to be extremely popular, and demand for these fellowships has continued to increase. In FY 1979, support was provided for 68 Senior International Fellowships. This number will drop to approximately 46 in FY 1980 and FY 1981. Funds will be sought in FY 1982 to restore the program to its FY 1979 level of 68 fellowships.

Scholars-In-Residence Program

The Fogarty Scholars-In-Residence Program provides a useful mechanism for attracting to the NIH outstanding scientists whose contributions foster valuable scientific exchange. Progress has been made in increasing the effectiveness of this program through efforts to encourage each scholar to plan and

develop specific work programs in advance of his or her period of residence at the NIH, to increase the participation of the scholars in the planning and conduct of conferences, seminars, and workshops, and to extend the degree of interaction of the scholars with the general NIH community.

Serious difficulties could be posed for scholars from certain countries if arbitrary requirements were posed for longer, uninterrupted periods of residence at the NIH. However, the FIC must explore ways to overcome or minimize those difficulties and to encourage the scholars to remain for longer periods at a time in an effort to further increase both the effectiveness and efficiency of the program.

Policy Studies Program

The report of the Task Force strongly recommended the creation of a Policy Studies Program to address issues and topics concerning the international aspects of biomedical and behavioral research, research manpower training, and the transfer of research results to health care systems. The FIC is according the highest priority to the development of such a program, patterned along the lines of the intramural programs of the Institutes.

The FIC will attempt to develop a small core of staff policy analysts and augment that staff by attracting staff fellows and individuals appointed through the Visiting Program and the Intergovernmental Personnel Act. In addition, an effort will be made to encourage Fogarty Scholars to participate in the conduct of policy studies and serve as an additional intellectual resource to the FIC through interaction with the staff of the Policy Studies Program.

The FIC will develop further the concept of the Policy Studies Program and will begin to structure the framework within which such a program can be implemented.

Conferences

The report of the Task Force raised questions concerning the appropriateness of the role of the FIC in the support of conferences and symposia and suggested that a return to traditional conference support through regular conference grants would result in a more orderly and systematic conference program. The Task Force recommended that the FIC withdraw from the general support of conferences and focus its activities on the initiation, planning, and conduct of meetings on topics directly related to international aspects of biomedical and behavioral research, especially those topics of direct concern to the Policy Studies Program.

The FIC has established a working group, with representation from several Institutes, to study the implications of that recommendation and suggest ways in which it may be implemented without creating a disruptive effect on the scientific community.

International Cooperation

Actions have been taken to strengthen the role of the FIC in coordinating the international activities of the categorical Institutes, providing a central focus for activities in support of NIH participation in bilateral agreements and other cooperative arrangements with foreign countries, and forging a link with other Federal health agencies and with the multilateral organizations responsible for directing broad international health efforts.

A professional staff person has been recruited for this function, a Committee of Institute representatives is being established to provide a forum for the exchange of information and views on international activities, and plans have been made to develop an improved data system for reporting the international activities of the NIH.

Chapter 15

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Chapter 15

NATIONAL LIBRARY OF MEDICINE

Director's Preface

Mission Emphasis

Efforts to improve human health are inevitably constrained by the extent and quality of the knowledge base from which they arise. In order to improve existing knowledge about health and disease and introduce new treatments and technologies into practice, new biological, behavioral, and medical knowledge must constantly be developed. This information must be organized and distributed to allow access by the user on a sustained basis in order to produce substantial lasting benefits. It is with this mission emphasis that the National Library of Medicine presents its current research, development and service programs.

The National Library of Medicine has identified four major objectives within its basic mission. These are:

1. The improvement of information and knowledge transfer for use by biomedical scientists and practitioners active in research, educational and health care delivery environments.

2. The establishment of an information base for scientists coupled with their resource requirements in an environment dedicated to the creation of a research center of excellence in biomedical communications in the new Lister Hill Center building.

3. The expansion and improvement of library and information services through the acquisition, preservation, organization, and dissemination of biomedical literature.

4. The improvement of information transfer for the protection of health through the provision of environmental toxicology information.

NLM and the Regional Medical Library Network

The National Library of Medicine is the focal point of the Regional Medical Library network. The provision of actual copies of the literature is accomplished by the nationwide Regional Medical Library (RML) Program of eleven Regional Medical Libraries, 102 resource libraries and 3,052 other health science libraries through the interlibrary loan system. NLM not only serves as the RML for Region IV but provides backup document delivery service in the event the other libraries in the system are unable to fill the request. In this way the NLM is an important resource for support of health research, education, and health care delivery.

The Lister Hill Center: The New Facility

The new Lister Hill Center building became fully operational in the spring of 1980. This magnificent new facility provides the long awaited laboratories and other resources needed to carry out the mandate of the Lister Hill National Center for Biomedical Communications, the National Medical Audiovisual Center, and other NLM support activities such as the Extramural Programs and the Toxicology Information Program.

Funding, Staffing and Expenditures

It is important to note that most NIH-funded research projects culminate in published results in professional journals which must be acquired, organized, and preserved for access and distribution by the NLM. The utilization of the NLM MEDLARS II system (Medical Literature Analysis and Retrieval System) has facilitated the distribution of this information for use by health care practitioners, researchers and educators throughout the world. However, the funding of the NLM must increase at a rate sufficient to handle the increasing volume of literature and its use.

Although funding for the NLM is important, the most critical problem facing the Library is the insufficient number of staff available to perform its labor-intensive mission. The volume of the literature and its use by the biomedical community of practitioners and scholars has vastly increased (110 percent) in the last ten years. In addition, since 1970 there have been increases of 86% in interlibrary loan requests filled, 78% in reader requests filled, and 65% in serials and monographs processed.

It is against this backgrop of resource requirements that NLM presents a plan dedicated to accommodating a portion of these staff deficiencies through the research, development, evaluation and use of new and creative ways of providing biomedical information to the health community. In a recent report to the Senate, the NLM estimated the additional positions needed to develop the interdisciplinary research team in the Lister Hill National Center for Biomedical Communications. The report also estimated the funds needed for personnel, equipment, services, contract support, and research grants of the Lister Hill Center.

The NLM also judges that additional funds and positions will be vital to pursuit of the MEDLARS III development effort, and to expanded activities of the National Medical Audiovisual Center, the Regional Medical Library Program, and toxicology information activities. The following plan provides a framework for the development of research to accomplish these objectives.

FY 1981 Program Changes

Objective #1: Improvement of Information Transfer

At the request of Congress (House Report No. 94-1093, May 6, 1976), the NLM is expanding information resources, document delivery, and on-line services for the health care delivery community. The important new initiative of

the NLM to explore and develop new methods for the transfer of clinically relevant information will be continued and expanded. It is neither possible nor desirable to attempt to accomplish this total research and development effort completely within the Lister Hill Center. The traditional NIH collaboration and support of independent research in the universities is as essential in addressing this problem as it is in any other biomedical endeavor. NLM therefore hopes to stabilize research grants which support the utilization of computers in medicine to solve problems in the fields of decision making, knowledge representation, indexing, automated information retrieval and related subjects and will provide support for the development of qualified investigators for research in biomedical communications.

Objective #2: Creation of a Center of Excellence for Research and Development in Biomedical Communications

General

The move of selected NLM programs into the new Lister Hill Center building during FY 1980 coincides with the completion of an extensive analysis and reshaping for the future of the Lister Hill National Center for Biomedical Communications' (LHC) research and development programs. LHC planning encompasses efforts to improve the manner in which biomedical libraries are used as well as to create wholly new and innovative information transfer systems. Ultimately, the purpose of information transfer is to provide the user with the underlying knowledge necessary to effect appropriate changes in the behavior of those in the health care delivery system.

The success of the development of the Lister Hill National Center for Biomedical Communications will be dependent upon the presence of an interdisciplinary research team with both a broad health science base and strong creative technology components, supplemented by visiting collaborating scientists from the biomedical and information science communities. A careful assessment of the personnel requirements to carry out these programs indicates a need for a significant increase in positions and funding for accomplishing the missions of the Center. More specifically, additional resources are required in FY 1982 to acquire an integrated research and development facility for exploring and demonstrating a modular approach to the synthesis of multimedia information packages from stored audio and high resolution video images. The electronically stored images might include material originally in the form of photographs and drawings, slides, film videotape, and hard copy text. The appropriate research, development and application of technology will become increasingly important as the results of collaborative efforts are carried back into the health science community and provide significant help in the practical solution of clinical problems.

The major Lister Hill Center programs include: (a) general studies of information transfer and knowledge utilization, (b) development of knowledge bases for medical science and practice, (c) the integrated library system, and (d) the document storage, preservation, retrieval and distribution system.

General Studies of Information Transfer and Knowledge Utilization

General studies of information transfer and knowledge utilization will focus on the following research areas: (a) the characterization and intellectual understanding of the organization and structure of formal and informal channels of communication, and their differential use by segments of the biomedical community (researchers, educators, and practitioners); (b) a study of the adoption and utilization by the biomedical community of advanced computer, electronic, and multimedia technologies that are intended to facilitate individual and group communication and education; (c) the application of cognitive theories of learning, decision making, and information processing applicable to the design and development of innovative information transfer mechanisms; and (d) the demonstration, testing, and evaluation of experimental information transfer methodologies and technologies.

Knowledge Base Program

The busy practitioner cannot be expected to process the mass of information likely to be available on a medical problem. Knowledge base systems have the potential to extend the practitioner's ability by providing effective analysis, synthesis and translation of the mass of information in a form and structure which make the information immediately available for solving day-to-day problems.

Such knowledge bases may be characterized as computer-based, condensed representations of published information. They may be organized in several levels of detail and contain citations to the original articles upon which the synthesis is based. They need to be kept current and should be capable of presenting graphics or illustrations to complement the text. They need to present the current state of knowledge as determined by the consensus of appropriate experts, and the user must be able to obtain the information he needs in a simple interactive fashion.

Integrated Library System

The goal of the National Library of Medicine is the effective transfer of health science information throughout the biomedical community. A major vehicle for achieving this goal is the network of biomedical libraries, ranging from local community hospitals to eleven Regional Medical Libraries and to the National Library of Medicine. As more libraries move toward automation, it is important that such actions proceed in a way which will build upon and strengthen this existing network structure.

The Integrated Library System (ILS) will make it possible for NLM and all other libraries regardless of size both to maintain computer-based data on local activities (e.g., indexing, cataloging, accounting and circulation), and to participate in automated support functions provided by regional and national library networks.

Document Storage, Preservation, Retrieval and Distribution

This program proposes to develop a document storage, retrieval, transmission and display system. This system will convert and store information contained in printed documents, film and machine-readable sources, and provide on-line retrieval for up to 4,000 typical journal issues stored on each optical disc. Techniques will be explored to develop a system capable of storing a thousand such discs with on-line access time of a few seconds. Such a system, if implemented, would be expected to occupy less than a hundred square feet of floor space, and store a collection equivalent to four million journal issues. If multiple systems are used, or if off-line operation is considered acceptable, the system capacity can be increased in proportion to the number of systems used and the physical area of storage space available.

The specific goal of this research program is the development of an experimental laboratory system to conduct research and development experiments in techniques for scanning, compression, storage, retrieval and display of interlibrary loan material. The long range goal of this program is to develop and implement a system to provide archival storage and nationwide electronic distribution of full text.

National Medical Audiovisual Center

The National Medical Audiovisual Center (NMAC) moved from Atlanta to the new Lister Hill Center building in Bethesda in March 1980. This move facilitates the improvement of previous service functions provided by NMAC and enhances the research activities conducted by its professional staff. The AVLINE program, NLM's on-line catalog of audiovisuals, will be enlarged from 7,799 references, as of October 1979, to over 10,000 references by FY 1982. New audiovisual technologies such as the use of videodisc systems and audio and video compression techniques will be explored. A program of research into various methods of distributing audiovisuals will be launched. In FY 1979, NMAC loaned 45,508 films and videotapes which were viewed by over 2 million people. NMAC will also evaluate a series of prototype workshops which focus on the training of faculty concerned with continuing education for health professionals. During FY 1982, this program will engage in an intensified outreach program to make training more readily accessible to as many individuals as possible who are charged with continuing education responsibilities for health professionals in the Nation's large hospitals, health science centers and other professional organizations.

Objective #3: Expansion and Improvement of Library and Information Services

The volume of biomedical literature doubles every twelve years. Coupled with this growth of literature has been the increase in literature acquisition costs of approximately 33 percent from FY 1977 to FY 1979. Concurrently there has been an increase in demand for biomedical information services which are highly labor-intensive tasks.

Planning to ameliorate this dilemma led to the MEDLARS III effort, a coherent library automation program which is directed toward satisfying the NLM's operational and service requirements for the 1980's. MEDLARS III is

intended to extend and improve MEDLARS II capabilities by integrating and augmenting the automation of bibliographic and other library functions which are being developed in several parts of the NLM. The implementation of this system will require extensive participation by NLM staff supplemented by outside contract support. The MEDLARS III development will necessitate a careful review of total resource requirements as well as the availability of services for similar systems at other institutions.

Development of a new automated MEDLARS III system will not be useful to the entire biomedical community without concurrent improvements in the Regional Medical Library (RML) network, which facilitates the transfer of biomedical information from NLM and the nation's large academic health sciences libraries to the local level. Additional funds will be required in FY 1982 to augment RML contracts and to allow for the growth and development of the network.

With regard to NLM's international program, there may be an increase in the number of countries relating to NLM under guid-pro-quo arrangements for international collaboration involving NLM's MEDLARS system, as well as an increase in the NLM data bases made available to these partners, with the NLM partner countries providing additional indexing in return.

Objective #4: Improve Information Transfer For the Protection of Health

The NLM will continue to collaborate with the health and environmental agencies on building the Chemical Substances Information Network (CSIN), proposed to Congress by the Council on Environmental Quality as a major step in implementing the Toxic Substances Control Act. With the additional $1,000,000 received as part of the FY 1980 NLM appropriation, NLM will be able to develop the Chemical Structure and Nomenclature System (CSNS), a key directory component of the CSIN. The CSNS is envisioned as an on-line chemical information search and retrieval system that will operate on a file of more than 1,000,000 chemical records.

Under the provisions of a previous agreement between NLM and the National Toxicology Program (NTP), the Library's Toxicology Information Program will provide NTP with: (a) literature-based information support regarding compounds selected by NTP for testing; (b) literature search support, as required, to assist NTP research and development; (c) assistance in disseminating information about NTP testing; and (d) technical direction for the NTP-sponsored Environmental Mutagen and Environmental Teratology Information Centers.

The Toxicology Data Bank (TDB) became available during FY 1979 as an on-line, interactive data retrieval service. The TDB contains evaluated data describing the chemical and biological properties, as well as the usage, environmental, and occupational characteristics of selected chemical substances that may be hazardous and/or whose exposure potential is significant. Data extracted from sources such as textbooks and handbooks are further evaluated by a peer review committee constituted from the NIH Toxicology Study Section which is comprised of pharmacologists, toxicologists and analytical

chemists. Additional funds will be needed in FY 1982 to improve the scope and coverage of the TDB for more effective utilization by biomedical researchers, particularly in the areas of neurological, behavioral, and fetal toxicology.

Summary

This document has described the critical role of the National Library of Medicine as a resource for health education, research, and practice in the 1980's. Given the necessary resources, the National Library of Medicine can become a center of research and development to facilitate information transfer, so that the discoveries in the biomedical research laboratories may more rapidly and effectively impact on the direct and immediate care of the patient. Without these resources its performance as the world's greatest specialized research library may be jeopardized.

Summary of NLM's Research Plan Review Session with the Director, NIH

National Trends in Medical Librarianship

The discussion opened with a review of the condition of libraries at many of the nation's medical schools, universities and other research institutions. Within the constrained budgets of many of these institutions, particularly the universities, libraries have little flexibility to improve facilities or to implement new operating methods. The result has been a gradual decline in innovation, a shrinkage in services, and an apparent growing dependence on NLM.

Through the Regional Medical Library network, NLM provides increasingly important services to the nation's medical libraries such as cataloging, indexing, bibliographic searches, and satisfying the growing volume of loan requests. These services to libraries and investigators are being augmented by a number of on-line information systems which can yield immediate information to clinicians for use in research, diagnosis and treatment.

The National Library of Medicine has been the leader in establishing new methods for providing medical literature services for some time now. Through increased use of computer-based data and text systems, a growing complement of search and transmission networks, and innovative techniques for storage and reproduction, the NLM is helping to broaden the capabilities of the nation's biomedical libraries.

Despite diverse machine capabilities, a human workforce is as necessary as ever. Many aspects of cataloging and indexing, for instance, are labor-intensive and have not yet yielded to attempts at automation. The ideal solution would be to replace indexing with text searching of the entire article. One encouraging step in this direction has been the inclusion of abstracts by the authors or editors for about 40% of the articles in MEDLINE. These abstracts also can be easily retrieved by the on-line searcher.

The services and programs of the NLM are clearly of great importance to the research institutions of the nation. Library facilities must be included in any assessment of the condition of the research apparatus in those institutions, as consideration is given to the most appropriate methods of research support for the future.

Stabilization of the Science Base

In the view of the NLM, the stabilization of NIH research grants would have an adverse impact on both the service and the research activities of NLM. NLM research grants are not protected by the stabilization plan, because they are quite different from traditional NIH research project grants. In the face of 15% per year increases in service loads, NLM with a level budget would have to absorb 10-15% increases in the cost of doing business.

NLM has recently emphasized the development of trained researchers in biomedical communications and the need for major studies in the use of computers in medicine. The new Computers in Medicine program made its first five awards in FY 1979. The explosion of technological advances in computing and

information sciences is widely recognized, and the pool of experts in these fields is expanding rapidly. The planned expansion of this effort could prove impossible without new money, and the relationship of such an expansion to the stabilization initiative is uncertain.

Services

A perennial issue in the management of NLM is how to achieve an optimal balance between services and research. Service demands are, of course, more pressing at present, but research advances in information handling are necessary to guarantee that future services can be efficiently delivered.

NLM's capacity to render services has been affected by a tight personnel situation. Processing of serials and monographs plateaued in 1976 at about 200,000 per year, and an increasing backlog now totals 10,000 items. The proportion of interlibrary loan requests filled has declined from 87% in 1976 to 85% in 1979.

The success of NLM's Medical Literature Analysis and Retrieval System (MEDLARS) is recognized throughout the biomedical community. Computer-based on-line retrieval services have been the fastest growing group of services provided by the Library. Since 1973, access to the retrieval system by the health community has grown from 180 to 1200 institutions. Similarly, computerized searches provided have risen from 165,000 to over 1.4 million in 1979. Because of a lack of computer capacity, it has been necessary to declare a moratorium on admittance of new institutional users, causing concern in the medical community. The range of on-line services offered, particularly the data bases applicable to health care delivery, have generated interest outside major research institutions, and many of the new applicants to use the systems are community hospitals and small academic institutions.

To place NLM's own service load in perspective, it was noted that libraries in each of the eleven regions fill an average of about 100,000 interlibrary loan requests per region per year--about half the number filled by NLM. Thus, despite the squeeze on service capabilities, NLM must continue to devote a portion of its resources to research, in order to continue improving the Regional Medical Library network and other network-based services.

Research Programs

A number of special needs for the period of FY 1981 to FY 1985 have been identified by the Library, to make the Lister Hill Center programs fully operational. These needs have been outlined in a special report submitted to Congress.

Another overriding management issue of the NLM is the weighing of intramural and extramural research opportunities. Much of the research within the mandates of the Lister Hill Center is currently pursued intramurally. The Computers in Medicine program shows particular promise for yielding high quality grant proposals and could be expected to yield practical results within a few years. Through grants, the skills of existing experts in the computer field could be focused on medical information problems in decision making (e.g. diagnosis), knowledge representation, indexing, and related topics.

This program may prove to be quite important to the Library's future, given the opportunities which exist in the field of computer sciences. Although the Division of Research Resources for a number of years has been supporting studies of the applications of artificial intelligence to medicine, the NLM and DRR have coordinated their efforts to assure that this new program will promote valuable contributions to the field.

National Medical Audiovisual Center

The move of the National Medical Audiovisual Center from Atlanta is complete. Twenty of the staff moved early in March, and about 52 vacancies will have to be filled, including the Director and three Branch Chiefs. Active recruitment is underway to attempt to fill these critical positions. It is anticipated that NMAC programs in development, utilization, and research related to health professional education materials will be resumed on a gradual basis.

Lister Hill Center Building

The new Lister Hill Center building has been completed. It houses the Lister Hill Center for Biomedical Communications, the National Medical Audiovisual Center, and much of the Fogarty International Center, as well as the following additional units of the NLM: Office of Computer and Communications Systems, Office of Contracts Management, Division of Extramural Programs, Division of Specialized Information Services, and the Bibliographic Services Division.

Major Civil Rights and Affirmative Action Initiatives

In an effort to provide career development opportunities for lower level employees, NLM has designated five special "career ladder" positions. Each position is set aside for applicants at a particular entry level and is intended to provide training and advancement within a special field.

A committee has been formed to locate minority candidates who can compete for positions to be filled in the National Medical Audiovisual Center. Special efforts continue in the hiring of handicapped employees, who now total 15.

Dr. S. Richardson Hill, Jr., and Mr. James F. Williams II attended the meeting on behalf of the NLM Board of Regents.

Chapter 16

CLINICAL CENTER

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Chapter 16

CLINICAL CENTER

Director's Preface

The overriding management challenge for the Clinical Center will be occupancy of the Ambulatory Care Research Facility (ACRF) beginning in FY 1982. In preparation for the utilization of clinic space in the ACRF, detailed proposals have been received from each Institute of new inpatient and outpatient programs and needs. Space will exist for these needs, but personnel remains a critical problem as it has in the past. However, in 1982, it will no longer be a question of underutilization of hospital beds because of personnel needs--the issue will be an inability to use one-half of a new building that was built for the express purpose of meeting the needs of increasing outpatient clinical research. It must be emphasized that the Clinical Center has absorbed many new responsibilities during the past two years without additional personnel and it will not be possible to staff ACRF adequately if the position levels in the 1980 and 1981 fiscal years continue into the 1982 fiscal year. The Clinical Center, therefore, is requesting additional positions to staff the ACRF.

In previous years, emphasis has been placed on meeting the need for new and increasing services, however, this focus is changing. The hospital has taken on more of the characteristics of a 24-hour, 7-day a week hospital, consonant with the requirements of patients and staff. Among the services initiated or expanded this year are the opening of the Medical Intensive Care Department, the initiation of the Gynecology and ENT Clinics in collaboration with the National Naval Medical Center, the expansion of the "pheresis" services, the development of space and personnel for positron emission tomography, and the expansion of the role of the CC in Clinical Associate recruitment. These changes have been accomplished without additional positions and in spite of shrinking space.

The continuation of this process of change, as seen by CC administration and as desired by Institute physicians, leads to an increasingly central role for the hospital. During this coming three year period, the CC will be asked to expand medical intensive care and to take major responsibility for surgical intensive care, to assume responsibility for almost all of the escalating needs for plasmapheresis and leukopheresis, to develop a central facility for inpatient and outpatient electrocardiography, EMG pulmonary function, echography and other functions, and to assume the responsibility for some interinstitute programs such as genetics. These are appropriate tasks for the CC, but they come during a time when it shall be pressed by a series of other commitments.

In addition to the above, the Clinical Center has accepted major responsibilities for the entire Building 10 facility. The Center is gradually assuming the role of a facility manager by providing materiel handling services throughout the building and by accepting the responsibility for safety of all

areas. The need for a facility manager becomes evident when one considers that Building 10 with the addition of the ACRF will contain over one-third of all space on the reservation and over half of all laboratories.

The above statements emphasize the increasingly central role occupied by the Clinical Center in its mission of support of clinical research and in its growing role of facility manager. New responsibilities will have to be accepted in the coming several years. With each of these comes the need for personnel and support. In each case, the Institutes benefit since they no longer have to devote so much of their resources to areas that are not clinical research *per se*.

ACRF/CC Modernization

ACRF occupancy and continuation of complementary Clinical Center modernization will highlight the FY 1982-84 period. Renovations prerequisite to ACRF occupancy will be completed by the close of fiscal year 1981. These will include Glassware and Media Preparation, Central Sterile Supply, Surgical Recovery/Intensive Care Unit, and both NHLBI and NCI Surgery Patient Care Units. ACRF occupancy will occur in fiscal year 1982 with the relocation of Diagnostic Radiology, Nuclear Medicine, Clinical Pathology, Surgery, and ambulatory clinics. Activation of the ACRF-based Clinical Research Service Center, Visitor's Center, and automated Materiel Handling Program will occur simultaneously. Vacated Clinical Center space will be filled in FY 1983 and thereafter by Rehabilitation Medicine, Medical Intensive Care Unit, Hemotherapy, Medical Records, Dental and Radiation Oncology clinics, and various administrative activities. Approximately three patient care units will be modernized annually throughout this period.

These extensive alterations will require new commitments by the Division of Engineering Services. Therefore, the personnel needs of this division must be addressed or the processes described above will not proceed in a timely fashion.

Medical Information System (MIS)

Full implementation of MIS in the outpatient department will be accomplished by January 1980. Just as the plan for ACRF highlighted the long-desired integration of inpatient and outpatient services for optimizing care, research, and staff efficiency, so does MIS offer for 1982 and beyond an integration of data communication, storage, retrieval, and archiving for CC services. The tasks of processing orders from 11 outpatient floors, in addition to 28 outpatient units, without a medical information system would be overwhelming even if staff increases were granted for manual processing. Having installed MIS, we now know these manual tasks would require many man-hours to achieve a level of service far below that being achieved currently. The reporting of data relating to patient care and research will be conducted with a timeliness and accuracy not approachable by manual or electromechanical means. The incorporation of these data in MIS will enable CC to maximize the use of the research data base and to simultaneously reduce the physical size of the medical record and increase its usefulness to the clinician and investigator. Finally, MIS exemplifies the CC as a network of interdependent functions whose effective management relies on rapid communication and clear channels of information.

A study of the costs and benefits of this medical information system is being initiated. Current contractual arrangements for MIS have posed limitations on our capacity to modify quickly components of the system. Pilot projects have been undertaken to examine the benefits that could accrue from collaboration between DCRT and the CC's Office of Clinical and Management Systems. Consideration is being given to alternative arrangements for managing the hardware and software involved in the medical information system.

Central Research Service Center

The Central Research Service Center (CRSC) located on the first floor of the new ACRF will house all the ancillary and support departments for both inpatients and outpatients. This section will be easily accessible and provide a central area for testing for patients. Currently, these functions are fragmented throughout the Clinical Center. This means the patients may spend most of their time traveling from one service to another. The CRSC will reduce the patient's time and provide a faster mechanism for reporting for test results. The CRSC will also be used for pre-admission tests for both inpatients and outpatients before they are either sent to the inpatient unit or to their respective clinics. The CRSC will house all the ancillary and support services except for Radiation Therapy and the Dental Clinic. Services will include phlebotomy, EKG, EEG, pulmonary function, ocular pressure room, audiology, and EMG.

Research

Clinical Center personnel are active in collaborative and service-oriented research and several of these areas have received national recognition. This is an appropriate activity for the Clinical Center and each outside review group that has reviewed our departments has recommended that CC research be encouraged and strengthened. During FY 1979, 124 scientific papers were contributed from six departments of the Clinical Center. Since research activities are often collaborative and generally service-oriented, individual departmental research budgets have not been requested. Nevertheless, these research efforts will be encouraged and supported and resources will be allocated to areas of promise.

Education

Education in the biomedical sciences is an essential component of biomedical research. The Clinical Center educational effort now involves coordination of undergraduate and postgraduate teaching, including continuing medical education certification which is required by professional societies and state boards of licensure. Cooperation between the Clinical Center and the component Institutes will continue to characterize expanded educational activities, and it is essential that the Office of the Associate Director act as the central resource for educational programs in the Clinical Center. Initiatives in this area will emphasize a joint effort to maximize the use of resources and to minimize duplication. It is likely that this will also involve local university departments where involvement of on-campus NIH educational activities is required. The development of an increasing number of shared teaching programs between the Clinical Center and the Uniformed Services University of the

Health Sciences can be foreseen. In order to compete for the outstanding student and potential research scientist, the Clinical Center must strive to offer training which will allow the maintenance of the appropriate medical skills while at the same time prepare the student to function as an independent investigator.

Program objectives, therefore, are: (1) education to support the research mission; (2) coordination and strengthening of existing interinstitute educational programs and development of new integrated training programs (endocrinology, clinical pharmacology, genetics, immunology and computer sciences); (3) the provision of continuing medical education to satisfy professional requirements; and (4) manpower development for biomedical research through involvement in undergraduate and postgraduate education.

The CC is currently in need of flexible teaching facilities. It must also reestablish the desirability of the NIH as a training facility and assume a leadership role in manpower development. This means the availability not only of space and equipment, but also the expanded use of outstanding lecturers from other universities and the availability of such resources as required for NIH to continue to present its benefits as a training site to students throughout the country.

FY 1981 Program Changes

There will be no significant program changes in the 1981 fiscal year. Because the level of positions in FY 1981 will be the same as in FY 1980, occupancy of the new ACRF clinics on the six tower floors will be delayed due to lack of staff.

FY 1982 Program Changes

The additional resources requested for FY 1982 are directly related to the occupancy of the Ambulatory Care Research Facility and, as noted previously, effective utilization of the ACRF depends on their availability.

Summary of CC's Research Plan Review Session with the Director, NIH

Management Issues

Some difficulties in managing and controlling the CC/ACRF facilities were indicated. The creation of the new Office of Research Services in OD and appointment of its Director will permit an examination of how these NIH central services are administratively organized and staffed.

Nursing

- Nurses represent 40% of the CC work force with a current turnover rate of about 24%. The CC feels that the nursing work force has achieved a high degree of operating efficiency by the use of intermittent appointment nurses to handle weekends and peaks in patient loads.

- The CC is fortunate to have an adequate supply of nursing staff, as many local hospitals are experiencing considerable problems in recruiting and retaining nurses. This is due in part to the CC's ability to offer competitive salaries to nurses, but also to the recognition demonstrated by the CC of the expanding role of nursing and the need to provide research opportunities and training.

Medical Information System

- The MIS is now a fully integrated and valuable part of the hospital and the laboratory link to the system has been made. A contract for an evaluation of the MIS has been placed out on bid. Future options that are being considered include CC acquisition of a computer and CC programming or programming performed jointly by the CC and DCRT.

- The Clinical Center has been working also with DCRT on integration of MIS research laboratory information into the Clinical Information Utility (CIU) System which would entail the transfer of on-line data to storage systems. The benefits of such an integrated system were demonstrated recently when a hypertensive drug recall notice was received by the CC. The MIS and CIU systems were queried and within 24 hours those patients currently taking the drug and those who had received the drug in the last six months were identified, and the dosage and length of drug treatment reported.

Clinical Center Initiatives and Issues

- Department Reviews--Ad hoc committees of experts have been reviewing CC departments with generally favorable results. It is the Center's view that CC departments should be involved in research and training, in addition to performing services, in order to retain a high caliber professional staff.

- Nutrition Research--There are currently 10 patients on metabolic diets in the CRNU in the hospital, with an increased interest in nutrition being reported by NHLBI research programs.

- Medical Intensive Care Unit--The MICU became operative last year within the constraints of existing personnel resources.

- Surgical Services--These activities have been reorganized and now fall under one group which does scheduling, administrative functions, and research services. The system, which includes three subsets of surgical nurses and pump technicians, is working very well.

- Anaesthesia Service--Anaesthesiology is continuing with the same group and leader. This contract service arrangement has been successful, but expensive.

- Protocol Review Committees--Each Institute subpanel now has two public members. The two levels of review, by the Institute and then the office of the Director, CC, have resulted in a review process of high quality that is capable of handling a large number of protocols, averaging 180 new protocols a year.

- New Initiatives--A nephrology service which performs renal biopsy and dialysis has become an important new CC service. An audiometry clinic has been started. The new gynecology clinic is jointly staffed by the CC and Navy. The new CC pheresis service, which includes leukopheresis and plasmapheresis, will require more positions in order to meet growing clinical demands.

Occupancy Rates/Staffing Needs

The length of stay in the CC has been declining from an average of 23 days in 1975 to 15 days in 1979. The occupancy ratio, however, has not changed significantly. Consequently, an increase in the number of patient admissions is occurring which, in turn, is resulting in an increased demand for hospital services. The CC is, therefore, currently in the position of providing more services with the same number of positions. It is the Clinical Center's view that productivity cannot be further improved beyond the present level of efficiency and that the CC is at a difficult point in balancing increasing patient needs and limited position ceilings.

Major Civil Rights and Affirmative Action Initiatives

- FY 1980 will be a transition year for CC affirmative action planning because of the emphasis to be placed on quantifiable results required by the Garcia Amendment. The CC will be establishing numerical targets for hiring minorities and women. Recent senior staff positions have been successfully filled in accordance with the CC Affirmative Action Plan. If additional positions are made available with the opening of the ACRF, the CC should be able to expand its minority representation.

- EEO responsibilities are now included in the merit pay provisions for GS 13 to 15 managers and supervisors, and the Clinical Center's EEO coordinator office will provide assistance in meeting these objectives.

- The CC has undertaken intensive efforts to increase minority recruitment for the Clinical Associate Program. The National Health Service Corps payback clause has been a problem with regard to this effort; however, steps are now being taken to modify this.

Education and Recruitment

- Continuing Medical Education--Record keeping is becoming more of an issue in CME; therefore, the CC is working toward meeting the documentation and educational needs of its staff. One option being considered is NIH sponsored, off-site programs.

- Clinical Associates--The numbers of applications received for clinical associates have been steadily increasing with the level of applicant quality being retained. The improvement in application numbers is due, in part, to a recent CC advertising program. Recruitment presentations oriented toward Institute research programs have been found by the CC to attract more M.D.-Ph.D. applicant interest. Although the current CC situation with regard to attracting young physicians into clinical research is satisfactory, concern was expressed about the national situation.

- Patient Education--Closed circuit TV (Clinical Center Television Channel 10) has been recently introduced by the CC for the education of patients on various health topics. In addition, a short film, "The Right to Know", on patients' rights and responsibilities in a research hospital and the booklet, "A Patient's Guide to Research at the Clinical Center" are both efforts by the CC in continuing to inform patients.

- "Medicine for the Layman"--This educational series for the public has proved to be quite successful, averaging 80% occupancy in Masur Auditorium. Therefore, the CC does not plan to extend present advertising efforts on radio and in local newspapers. A measure of success is the inquiries received by the CC from the public and medical institutions about this series.

Ambulatory Care Research Facility

The schedule for completion of the ACRF is on target and any delays that may occur will probably be a result of changes in plans for CC modernization. Although the ACRF building will not be turned over to the CC until April, 1982, beneficial occupancy of some ACRF laboratories may begin as early as March, 1981.

The large number of positions requested by CC departments which would represent optimal use of the ACRF was discussed. As originally planned, this use would include an outpatient load growing from a 6% increase to a 10% increase annually, and staff for the clinical research service center and other needs. Contingency plans have been prepared which include information on the minimal number of positions (mostly service staff) that would be required to open the facility and on the services that could be provided with various intermediate staffing levels.

Chapter 17

DIVISION OF RESEARCH SERVICES

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Chapter 17

DIVISION OF RESEARCH SERVICES

Director's Preface

More effective and efficient research support can contribute in an important way toward the goal of maintaining high quality biomedical research. The Division of Research Services (DRS) has a unique opportunity to develop models of support services which can lead to greater efficiency. In some instances the union of intramural and extramural activities has resulted in more cost-effective research support for the biomedical research community. An example is the coordination of the development of primate supply programs by the Interagency Primate Steering Committee (IPSC).

Other recent examples of DRS leadership in developing new and improved approaches to research support include: (1) establishment of a central scientific equipment rental pool to make research instruments available more readily, efficiently, and economically; (2) creation of a central microanalytic facility to develop new techniques and make them available to all NIH researchers; (3) expanded application of bioengineering to clinical research; (4) the development of improved technology for the safe handling of infectious organisms and hazardous agents in the research laboratory; (5) improved methods of utilizing and disposing of radioisotopes essential in research and clinical care; (6) improved methods for monitoring the genetic purity of strains of research animals; (7) formulation of standardized laboratory animal diets which are being widely used throughout the scientific community; and (8) the breeding of several strains of animals to meet specific research needs.

Because of its size, and the excellence of its research, the NIH intramural program offers a unique opportunity for the development of improved research services. When combined with resource support for extramural activities, the benefits are extended to both areas. For example, within the past two years we have developed a system which provides foundation animals from our genetic resource to commercial breeders who supply animals for National Cancer Institute contracts to test chemotherapeutic agents. We, in turn, also buy animals from some of the same suppliers for intramural investigators. We perform quality controls on these animals which benefit NCI programs as well as NIH intramural research. The scale of the entire system has reduced many unit costs. There is now greater uniformity for both programs, and research results can be more realistically compared. Overall this has resulted not only in greater effectiveness, but also greater efficiency.

By FY 1982 the Divison of Research Services should be making much greater efforts to extend the intramural/extramural collaboration in both the bioengineering and animal resource programs.

By FY 1982 completion of the Ambulatory Care Research Facility can be expected to place more demands on the Division. Indications are that

additional resources will be needed to meet new requirements and added responsibilities.

DRS has continued to maintain a high level of service and to improve technology in those areas for which it is responsible through greater efficiency, increased contracting, and the use of overtime.

FY 1981 Program Changes

Attention should be given to reconditioning the facilities which remain on campus. Firm construction and renovation plans must be completed for upgraded facilities for barrier production and research holding and for bioengineering.

FY 1982 Program Changes

The quantitative elemental microanalysis facility has been initiated in a limited way and will continue. Components have been purchased, installed, and preliminary use has begun. Additional resources will be required for this activity.

Programs in pharmacokinetics, transport phenomena, and instrumentation and measurement techniques will be given high priority. Pharmacokinetics is becoming one of the best approaches to rational assessment of risk posed by low doses of environmental contaminants. The development of the optic probe has great potential for measuring large numbers of microscopic dynamic processes.

The Scientific Equipment Rental Program (SERP) has proven to be popular with NIH scientists. The inventory has been greatly expanded through the use of funds from the capitol equipment budget. There is an approximate 85% utilization rate of newly purchased equipment. Introduction of new types of equipment is in response to specific investigator requests and is reviewed before purchase to assure a demand beyond usage by the original requestor.

All of the aforementioned activities are of importance not only to the NIH intramural but also the extramural programs. In addition, the library and medical arts and photography activities have provided vital services to the NIH intramural programs. In these areas too, there has been innovation and progress which has enhanced the image of NIH. The technical expertise in the various DRS components can be expected to continue making important contributions which will help advance biomedical research.

Summary of DRS' Reseach Plan Review Session with the Director, NIH

Your presentation reminded us all of the important services DRS provides to the NIH community and the constraints your Division must deal with while maintaining the same high level of quality which has become associated with your operation.

Consensus Development Conference

The consensus development conference on "The Use of Microprocessor-Based Intelligent Machines in Patient Care" held last October was quite successful. The relative inexpensiveness and miniaturization of microcomputers have already led to the development of many new medical technologies. Among the most interesting technologies may be those resulting from the incorporation of microcomputers into familiar medical devices. The conference addressed a variety of issues which the use of such devices in patient care raises. A summary of the conference is available and that a fuller publication is currently under development. The conference was well represented by both the biomedical community and industry, as well as many different Federal agencies, such as NBS, NASA, and NSF.

Handling of Low Level Radioactive Waste

Although responsibility for this area now resides in the new Division of Safety, problems in the handling of low level radioactive waste were discussed. Recent public concern in this area, coupled with problems being encountered in the disposal of radioactive waste, makes it imperative that NIH carefully examine the current status of its handling of radioactive waste, develop contingency plans in the event that current procedures become unavailable in the future, examine alternative approaches that could lead to improvements in this area, and consider what role the NIH should play in considering this problem on a broader scale. Data maintained on radiation safety services provided for the receipt and processing of millicuries of radioactive material indicate a reasonable steady annual use of radioisotopes in the intramural programs. The Director of the newly established Division of Safety should take the initiative in dealing with these questions.

Renovation of DRS Facilities

Needs for the construction and/or renovation of DRS facilities over the next several years were discussed. These include:

- Addition of two wings to Building 102 at the animal center in Poolesville--This will serve as replacement space for Building T-8, temporary space which is in very poor condition.

- Extension to two wings of Building 100 at the animal center in Poolesville--This is required to house additional livestock and to control disease problems in certain herds.

- Outdoor kennels near Building 28--Current holding space for dogs and other large animals is inadequate, forcing investigators to defer projects and reduce the scope of studies.

- New facility for the Genetic Resource Center, to be located at Poolesville--In order to meet program needs and to comply with the NIH Master Plan, this unit must be relocated.

- Selected renovations of Building 14 complex and possible construction of animal holding facility--This item involves many different program areas and temporary moves in order to properly upgrade space for many of the DRS operations.

Biomedical Engineering and Instrumentation

The discussion centered on the operation of the Scientific Equipment Rental Program and the need for a more integrated, collective NIH approach in the area of biomedical engineering.

-- Scientific Equipment Rental Program

1. In the past year this program has expanded. With an increase in funding, it has been possible to add pieces of equipment to the pool. The number of items rented in 1979 has almost doubled from previous years.

2. Utilization of equipment is running around 80% over-all. The rental rate is now 2% per month of the new purchase price. DRS provides maintenance and repair of equipment at no cost. Most investigators are now going to their Scientific Directors for approval prior to requesting rental. Requested items costing over $25,000 are purchased for the Rental Program if (1) the investigator signs a rental agreement, and (2) other NIH programs will be able to utilize the items in the future.

DRS is to be commended on this well conceived and well managed program.

-- Biomedical Engineering

1. The Division serves as the focal point for expertise in this area at the NIH. We agreed that this is an area that requires greater coordination here at the NIH and also with the many other Federal agencies concerned with biomedical engineering.

2. Action should proceed your proposal to create an NIH working group which will develop a serviceable definition of biomedical engineering, inventory NIH activities in this area, identify gaps and explore possible approaches for interagency coordination.

Library and Medical Arts and Photography

The automation of certain library services is proceeding well and a number of additional data bases are being added to the system. The Medicine for Layman series handled by MAPB represents a superior publication and should be widely distributed.

Animal Resources

The supply of primates continues to be a problem. Most source countries are not exporting primates, and this situation is not expected to change dramatically in the future. High priority be attached to our domestic breeding programs so that we can eventually reach self-sufficiency. The breeding program with PAHO is operating well and efforts to enter into collaborative arrangements with WHO should continue.

Affirmative Action

Initiatives in this area include:

- The development of an Affirmative Action Plan which is now out for employee comment. This plan will be published soon and widely distributed.

- Additional supervisory training has been provided and there continues to be some growth in minority representation in Division positions.

Chapter 18

DIVISION OF COMPUTER RESEARCH AND TECHNOLOGY

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Chapter 18

DIVISION OF COMPUTER RESEARCH AND TECHNOLOGY

Director's Preface

During its fifteen year existence, the Division of Computer Research and Technology has become an integral and vital part of the NIH. Its multidisciplinary expertise--in the physical, mathematical, computer, and life sciences--has enabled NIH clinical collaborators and administrators to use the powerful emerging computing technology. The Division's integrated research and development program serves all of the BIDs and the OD, NIH.

Clearly, the demand for highly developed skill in data processing and its associated disciplines will increase during the period of austerity that is expected in the Federal sector during the next several years. The use of the computer certainly will assist in providing efficient and effective programmatic support to all facets of NIH, to help compensate for manpower losses.

The Clinical Information Utility and the Material Management System are two classic examples of long-term collaborative efforts between DCRT staff and others in the NIH community.

The Clinical Information Utility is a clinical information data base technology developed through the Data Management Branch's work with the Clinical Center's Office of Clinical and Management Systems over the last six years. This system has allowed 170 NIH clinical scientists to retrieve specific kinds of data from some 15 million test results recorded by Clinical Center clinical laboratories. During FY 1979 the Office of the Director, Clinical Center has used the technology to improve medical records for support of patient care by all NIH clinical services. Collaboration has begun with the DCRT Laboratory of Statistical and Mathematical Methodology to provide improved facilities for building and analyzing subsets of clinical research data.

The Material Management System now is capable of: (1) handling all purchase, receiving, and payment functions at point of transaction; (2) making all entered data available to all central NIH offices; (3) providing both regular and exception reports in on-line and batch modes; (4) preparing file reference and reminder information automatically for out-of-sequence events; (5) generating purchase order documents and tracking purchase order number assignments. Several enhancements to the existing system have been identified, and will be implemented in stages, as manpower permits.

DCRT's continuing support touches other areas, as well. Current planning calls for the completion of the two major reprocurements of the central NIH computing facility by 1982. The years leading up to this point will require extreme dedication and effort by the staff due to the manpower reductions in the DCRT Laboratories and Branches.

DCRT hopes to continue affirmative action efforts in employment. Currently, seven handicapped employees are performing in an exceptional manner. A special effort in this area began in July, 1978, when the Data Management Branch hired a part-time computer technician with the understanding that he would perform all of his work from his bed at home. He is a quadriplegic who, after extensive assistance from the Virginia State Rehabilitation Service, learned to program by way of a voice data entry system. When the Division hired him, it assumed the task of adapting this voice entry system to function with the NIH IBM-370 system. A collaborative effort resulted in a vocabulary, a training program, and an interface program which enable him to have voice communication with the NIH computer facility. Although this effort was initiated primarily for one person, DCRT is now examining alternative voice entry hardware and potential new applications for this approach to data entry and programming.

A prototype voice output terminal system has been developed using a microcomputer and speech synthesizer in combination with standard computer equipment. The system allows a blind programmer to have full comprehension of computer output and, therefore, programming independence.

An in-depth analysis conducted this year of the 334 series, which is the majority workforce of DCRT, showed that the Division equals or exceeds the National Relative Labor Market percentage for women. As attrition permits, affirmative efforts will continue in this area to increase the other minority total.

An active search is underway to hire "experts" for highly specialized research efforts in several areas such as molecular dynamics of large biological structures, theoretical analysis of cell locomotion, and pulmonary physiology. It is intended that their research efforts will bear fruit during the 1982-1984 time frame.

Being named a Federal Data Processing Center has presented no problems for DCRT. Several new statistical customers are using the central facility; this sharing effort, and the resulting reductions in the cost of computing, are of direct benefit to NIH.

Several potential major problems face DCRT in its Future Plans. These include, in part, such things as:

- Possible need for additional funds to purchase computer equipment, as a result of the ongoing reprocurement. The Division also expects a Delegation of Procurement Authority for the 370 system procurement and will need an NIH Contracting Officer who can provide a major effort in this activity.

- The 370 system is currently being utilized to almost 100 percent capacity; due to possible delays in the installation of equipment under the ongoing reprocurement, it may be necessary to request an interim upgrade in capacity.

- Additional manpower and space needs as a result of the increased service demands of the BIDs.

- Need for an uninterruptable power supply to protect the integrity of the data processed by the central computer facility.

- The new ADP Systems Security plan clearly will have a profound impact on DCRT and all of NIH if implemented as written.

FY 1981 Program Changes

DCRT's program plans will be difficult to assess during FY 1981. No major program changes are planned for FY 1981 and the Division will continue its efforts at current or reduced levels contingent upon what demands may occur. Several efforts will continue as indicated.

Data Base Management

Full implementation of phase III of the Material Management System was scheduled for completion by 1981. This would include such activity as requisitioning entry, full fund certification and approval, and central stores inventory and ordering. However, the recent personnel cuts have produced serious problems with this time frame, although NIH should be approaching a full data base management system during this period.

Clinical Information Utility

The Clinical Information Utility (CIU) is a Data Base Management System that collects, organizes, archives, and retrieves clinical data. The CIU System permits research investigators and managers to obtain clinical data for research and administrative uses.

This system collects clinical data from three major data sources: the Clinical Laboratory System, the Medical Information System, and the Medical Records System. The following data bases are maintained by CIU:

- Clinical Laboratory Data

  Chemistry and Hematology
  Microbiology
  Bone Marrow

- Medical Information Data

  Medications
  Vital Signs
  Admissions
  Biographical

- Medical Records Data

  Discharge Diagnoses

Generally, clinical data are retrieved with a user-defined patient set: a list of hospital numbers. By using the hospital numbers to select records, all data or subsets of clinical data can be retrieved from each of the data bases in the form of a printed report, magnetic tape, microfiche, a Patient Profile Report, or through descriptive statistics, including means, frequency tables, standard deviations and variances.

Image Processing

Recent developments in, and increased usage of computer graphic techniques by the BIDs for an ever wider array of chemical and medical images may require a major effort in developing "packaged" software for the Surface Display and Digitizing facility run by the DCRT. A task force is being considered to address this problem; the results of their study should be available in 1981. This effort will involve a significant amount of manpower and dollars and may therefore require additional positions. This facility needs additional machine space, but this situation should be resolved when the work on the fourth floor of Building 12A is completed.

One current use of image processing is to display and aid investigators in perceiving the spatial relationships between atoms; this has led to a better understanding of the structure of the active sites of proteins. Graphics of the structure of immunoglobulin and collagen are being finished, and work is in progress on the structure and activity of insulin. The DCRT staff, in collaboration with the National Cancer Institute, also is using the system to process whole-body Computerized Axial Tomography scans in an effort to improve planning of radiation treatment for cancer.

FY 1982 Program Changes

The state of the art of computing in the 1980's is a subject for continuing debate in the industry and in academia. The rapid rate of technological development in the areas of computer science, engineering, and electronics is almost overwhelming. Predicting what the future may hold for DCRT is thus difficult. It is certain that ongoing programs in the areas of image processing, data base management, and clinical information processing will have matured in the 1980's.

The large NIH Administrative Management Systems should be in a true data base management environment at that point in time. The NIH data base will include the Material Management System and the Central Accounting System, and will provide all necessary data to provide an interface with the Management Accounting Network of the Department of Health and Human Services. The potential will also exist to capture all grant award information; this system would be capable of providing information and reports to all levels of management via terminal query.

The Clinical Information Utility originally was programmed to collect clinical data for research use by individual investigators. Overtures have been received from the Clinical Center to expand this system to collect data for the medical record and for patient care use. If this evolution occurs,

the opening of the Ambulatory Care Research Facility will have a significant impact on the volume of data collected by the system. From DCRT's viewpoint, this could create serious problems in the storage and processing of data, due to the lack of sufficient staff in several program areas.

We plan to continue our efforts over a broad range of activities that include the following:

- Develop, test, and improve mathematical models of physiological processes.
- Develop and apply statistical theory and computer programming systems to create new techniques for diagnosis and evaluation of disease, and for assessment of the effects of treatment.
- Engage in independent research in applied mathematics, statistics, and computer systems necessary to provide a sound theoretical basis for methods used in collaborative studies.
- Provide research, development, and consultation for the design and implementation of project-supporting computer systems.
- Develop statistical and mathematical theories for computer implementation of quantitative methods in biomedical research.

All of the above program efforts are, of course, contingent upon the availability of appropriate manpower. Staff shortage is the Division's most serious problem.

Summary of DCRT's Research Plan Review Session with the Director, NIH

1980 Research Highlights

A number of research trends and achievements were cited:

- Computer-based "voice technology" has been a subject of study due to DCRT's special efforts to employ handicapped persons. A special voice data entry system has been adapted to assist a quadriplegic computer programmer in operating the IBM-370 system. A related effort has led to development of a prototype voice output terminal system, allowing a blind programmer full programming independence. These efforts, while initiated for the handicapped, are leading to applications of this equipment for the non-handicapped as well. Studies show that the use of this technology brings parity in the workplace for both handicapped and non-handicapped computer programmers.

- Development of multipurpose integrated computer input/output systems utilizing microprocessors is a special initiative. Each system will be capable of accepting information in several different formats, and producing information in a variety of formats.

  A variety of instruments are used in laboratories, clinics, and offices, such as: conventional typewriters and special purpose keyboards, transducers with their digital voltmeters, and bar code and scanning wards, in addition to voice input/output.

- The WYLBUR text editor has been used by NIH authors to produce magnetic tape versions of journal article manuscripts. Such tapes can be read directly into typesetting computers of most major printers, eliminating the usual retyping by the printers and the galley proof step. This technology should eventually be capable of producing manuscripts for any journal, thereby saving typesetting time and costs, as well as guaranteeing fidelity of the author's manuscript.

Data Base Technology

In recent years, DCRT has been employing the principles of data base technology to improve the efficiency and usefulness of the largest NIH data bases. This technology separates input/output procedures and programming from the data files, and combines all data files into common data bases. The Clinical Information Utility System, Material Management System and a part of the Financial Management System are being established with data base technology. Advanced design principles called data base management technology are now being applied, to further refine the systems.

Clinical Information Utility

The Clinical Information Utility System (CIU) was established as a bank of clinical data on patients of the Clinical Center, to integrate several automated files of clinical laboratory test data and medical records data, such as discharge diagnoses. DCRT's Data Management Branch and the Office of Clinical and Management Systems of the Clinical Center are working on additions to the system, and in particular, to incorporate data from the Medical Information System into it.

Use of the CIU System has been largely for clinical research purposes, with the Office of Clinical and Management Systems controlling all access to the system and aiding investigators in conducting searches. Further work is underway in cooperation with the Clinical Center to supplement the handling of ad hoc queries by developing a number of reports in support of clinical management of patients, and by working toward the establishment of disease-oriented data bases.

Central Administrative Systems

One of the most demanding new responsibilities for the NIH has been the multi-year task of developing and implementing an Administrative Data Base Management System, in cooperation with the Division of Financial Management and the Division of Administrative Services. This includes automation of the Material Management Systems (MMS) and the automation of the Financial Management System. Included in the automation of the Financial Management System will be the conversion of the Central Accounting System (CAS), a system for budget information and control, provision for BID access to the data base, etc.

During the past year, DCRT has successfully implemented parts of the receiving and payment segments of the data base system. Full implementation of the receiving and payment segments should be accomplished in FY 1980 with the completion of the delegated procurement and receiving portion and the invoice entry portion. During FY 1980 work will begin on Phase III of the data base system, which will include requisitioning, fund control, stock inventories, and conversion to the Financial Management System.

Reprocurement of Central Computer System

The reprocurement of both the IBM System 370 and the DEC-10 components of the NIH Central Computer Utility has progressed to completion of the first major phase--formal release of the specifications and the Requests for Proposals, representing almost three years of negotiations and intense effort. Much remains to be done. Proposals received in May 1980 will be followed by benchmark testing and negotiations, with a final award possibly scheduled to be made in January 1981. Installation should progress in stages through 1981, with the full system becoming operational by January 1982. This timetable is quite optimistic however, presuming that none of a wide range of possible delays occurs.

Major Civil Rights and Affirmative Action Initiatives

DCRT continues to work to increase its female and minority staff ratios, despite a serious shortage of women college graduates in the computer science and engineering fields. Particular attention has been given to hiring handicapped persons, with eight currently employed.

SPECIAL REVIEW SESSIONS

In addition to the annual review which the Director, NIH holds with each Bureau, Institute, Division and trans-NIH committee, occasional special reviews are conducted. These sessions focus upon topics of current interest or overviews of organizations not otherwise included in the annual reviews.

During the past year there has been considerable discussion of grants peer review processes, award rates and other subjects under the purview of the Division of Research Grants. A special review session was held to discuss these subjects as well as the Division's progress in responding to many new demands.

The recent establishment of the Division of Safety, within the new Office of Research Services, has provided a new focus for NIH efforts in the areas of radiation safety, occupational safety and health, and environmental protection. A special review session was conducted to discuss the plans for the new Division and NIH safety and environmental protection issues.

Summaries of the review session memoranda for these two organizations follow.

Chapter 19

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Summary of DRG's Special Review Session with the Director, NIH

Though pressed by rising demands, DRG has accommodated well to its changing environment. Actions effected and others being considered may satisfy many demands within DRG's present resources. Where this proves impossible special consideration will be given to Division requests for assistance.

Referral and Review Workload

The greatest challenge to management and peer review quality in recent years has been an increase in numbers of grant applications received annually. From 1974 through 1977, an explosive growth rate in applications culminated in an annual workload virtually double that of earlier periods. New administrative requirements have also added to the work of DRG and the study sections. Since 1977, however, there has been only a slight overall annual growth.

Establishment of New Study Sections

Existing study sections have absorbed this additional workload with relatively little relief, and DRG wishes to charter more study sections. The number of study sections now stands at 54, including the four established in February 1979--the first additions since 1975. Fifteen additional study section charters have been proposed or are being developed. Five of these are now under consideration by OMB, and three more developed by DRG for review of fellowship applications are to be submitted soon.

DRG Services for Non-NIH Components

A report on the type and amount of service which DRG renders to PHS components outside of NIH will be prepared for the Director, NIH. Referrals for FY 1979 and the first two rounds of this year may be expressed as follows:

Average Referrals per Review Round FY 1979-1980*

DRG Referral Branch Total	8484 grants	100%
DRG Review	6155	72.5
BID Review	839	10.0
Other PHS Review	1490	17.5

* Represents the first two review rounds of FY 1980.

Management Accommodation of Workload

A number of management actions by DRG and the NIH have been taken to mitigate the effects of the increased workload:

- An increase in ceiling from 400 in FY 1978 to 428 in FY 1980 has provided a measure of relief. Most of these positions have been devoted to the scientific review and referral functions, and over the past several years approximately 13 other positions have been internally reallocated to the review and referral functions. From FY 1975 to FY 1980, positions devoted to those functions have increased by 49.

- Meetings were arranged for Chairpersons of all NIH initial review groups to discuss issues and concerns and to help them better understand the system.

- The redesigned application form NIH-398 should result in smaller applications, facilitating review. Redesign of the application package to permit a single printing and assembly operation will save clerical time in DRG.

- The Concensor voting apparatus, tested in the ad hoc fellowship review groups during the June review round, should facilitate voting, aid tabulation, and highlight applications requiring further discussion.

- Several Executive Secretaries are experimenting with word processing and microfiche equipment to speed up summary statement preparation and facilitate handling and reproduction of applications and summary statements.

Management Information Services

The Division's Statistics and Analysis Branch and Research Analysis and Evaluation Branch have both been very busy, in part because of increased Department and Congressional interest in grants review and award procedures. Recent information demands include:

- Data for President's Budget: Breakdowns of FY 1979 obligations, priority score distributions of competing research project grant awards, and various payline estimates.

- Stabilization Models: Development of this initiative involved preparation of numerous models and computations.

- Congressionally Mandated Studies: The study of peer review, priority scores and normalization, conducted at the request of the House Appropriations Committee, was based upon a significant amount of data specially prepared by SAB. A more limited study of peer review of nutrition research proposals has been requested by the Nutrition Subcommittee of the Senate Committee on Agriculture, Nutrition and Forestry.

- BID SATT Codes for Projects: Work is continuing on procedures to record SATT codes for each grant and contract.

- Recombinant DNA Projects File: Work has begun on establishment of a file of key information on current and past NIH-funded projects involving recombinant DNA.

- Clinical Trials Inventory: Production of the inventory continues to be a major project of the Reports Analysis and Evaluation Branch.

- Award Rates: During the past year, problems with award rate data submitted to the Congress pointed to the need for a better system of reporting award rates. DRG staff spent a considerable amount of time preparing a data base and procedures for computing award rates.

Grant Applicant Investigator File

A major project of the Research Analysis and Evaluation Branch during the past year has been the development of a Grant Applicant Investigator File and production of analyses from the data. The new data base gives DRG the ability to perform studies requiring access to longitudinal data about individual investigators' histories of research support and training support.

New Departmental Management Accounting Network

The new Management Accounting Network to be established in the Department may place special demands on DRG in the next few years. A new Standard Accounting System for the Department is scheduled for implementation in 1981. A total redesign of the present grant payment system into a Payment Management System is also planned, to be implemented by January 1983.

Budget

DRG's budget for direct operations totals about $14.2 million in FY 1980, and has changed little over the last few years. About three quarters of this cost is now salaries. DCRT has helped DRG to keep costs down; within the past five years computer services costs have decreased from 14% to 8% of DRG's budget.

Travel

Due to increasing travel costs in recent years, the proportion of competing applications given site visits has gradually declined from 10.6% in 1968 to 1.5% in 1980. In the last year alone, 15% fewer people have travelled, while the average cost per trip has risen by 22% for site visits and by 36% for all travel. In order to provide adequate site visiting, the Division has requested and received a significant increase in its travel ceiling.

Civil Rights and Affirmative Action Initiatives

Significant progress has been made during the past year in recruiting women and minorities as Executive Secretaries, with the proportion of both increasing. The Division is attempting to set up a "hot line" in the Office of Grants Inquiries to give special attention to women and minority institutions.

Chapter 20

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DIVISION OF SAFETY

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Summary of Safety and Environmental Protection Issues Special Review Session with the Director, NIH

A number of current issues in the area of environmental protection and safety were outlined. The establishment of the new Division of Safety demonstrates the NIH concern and commitment to resolving these issues. The pursuit of an integrative approach which relies on the NIH community and B/I/Ds, and defines the Division of Safety as a catalyst and provider of resources to achieve safety and environmental protection goals is supported as the most effective way to proceed and probably the most feasible method considering the complexity of the tasks. A consensus development approach to the establishment of safety policy is advocated by the Division. To achieve this, the establishment of an Executive Board which will recommend policies to the Director, NIH, and three committees designed to address issues arising from the areas of radiation safety, occupational safety and health, and environmental protection is under consideration.

Radiation Safety Issues

Most of NIH's use of ionizing radiation is controlled and licensed by the Nuclear Regulatory Commission. This license requires NIH to have a radiation safety committee and a safety organization which has training and monitoring responsibilities. The NIH Radiation Committee and the Radiation Safety Branch fulfill these two requirements. Some of the issues with respect to radiation regulation which NIH must consider include:

- The use of P32 at NIH is increasing both in regard to the number of users and the maximum activity used per experiment. This particular radionuclide is considered more hazardous than other radionuclides generally used in biomedical research.

- NIH has adopted the concept of ALARA (as low as reasonably achievable) with respect to managing radiation safety. This requires NIH to strive to achieve safety levels beyond the minimum regulatory standards, an effort which tends to consume considerable manpower resources.

- EPA regulations to control radiation levels in air effluents are anticipated soon, as well as other regulatory initiatives which cover water and other emissions. These regulations will have an impact on NIH in its use of radiation and consideration of methods for disposal of low-level radioactive wastes.

Occupational Safety and Health Issues

Executive Order 12196 reaffirms NIH's obligation to establish an occupational safety and health program and to comply with existing Occupational Safety and Health Agency physical safety and health effects standards or to promulgate equivalent standards approved by the Secretary of Labor. An occupational safety program currently exists and is managed by the Occupational Safety and Health Branch, DS. The OSHB compliance program is evolving; one

goal is to strengthen technical resources available to the NIH community. Another goal is to develop a clear policy statement to guide NIH in the area of occupational health and safety. Some issues that were highlighted in our discussion were:

- Chemical Carcinogen Standards--The Subcommittee on Laboratory Chemical Carcinogen Safety Standards of the Departmental Coordinating Committee for Environmental and Related Programs (CCERP) has developed generic guidelines for the use of chemical carcinogens in DHHS laboratories. These guidelines identify four factors to be considered at the operational level in determining, on a case by case basis, safeguards for the use of chemical carcinogens:

  1. quantity to be used

  2. carcinogenic potency

  3. other physical and chemical properties of the material

  4. manner in which material would be used

  The draft guidelines will be reviewed by NIH before presentation to the CCERP. Subsequent plans call for the guidelines to be transmitted to OASH for consideration of formal adoption by the Department. It is hoped that these guidelines will serve to positively influence future OSHA regulations on chemical carcinogens for laboratory use.

- OSHA Inspections--OSHA now has the authority to conduct unannounced inspections of Federal agencies, if the agency does not have an OSHA approved occupational health and safety committee. NIH is in the process of establishing such a committee. Currently, clarification is being sought with regard to membership.

Environmental Protection Issues

The Environmental Protection Branch addresses environmental concerns covered by Federal laws, Executive Orders, and numerous State and local environmental protection and pollution control laws. Of these, four major laws have particular significance for NIH: National Environmental Policy Act (NEPA), Resource Conservation and Recovery Act (RCRA), Federal Water Pollution Control Act (Clean Water) and Clean Air Act. Some issues that have arisen from these areas are:

- NEPA--In accordance with the new regulations issued by the Council on Environmental Quality, the Department has recently proposed new implementing regulations (GAM - Chapter 30). While this set of regulations is more flexible than previous Department rules, some points are still unclear. Procedures will be developed by NIH, as necessary, to fulfill the requirements of NEPA.

- RCRA--Authority for implementing this Act, which covers waste storage, transportation and disposal, is delegated to States. Maryland has developed stringent regulations for hazardous waste disposal. The Division would like to explore new approaches in managing hazardous materials, including the possibility of on-site, environmentally sound disposal methods.

- Clean Water--The Act requires that special measures be taken to prevent inadvertent discharges of hazardous materials to surface and ground waters and to community sewer systems. Measures appropriate for NIH will be proposed by the Division.

- Clean Air--New EPA requirements are anticipated which would control atmospheric discharges of specific hazardous chemicals. Such action may require a reevaluation of current NIH discharge methods.

Safety Training and Information

The Division is developing a variety of approaches to achieve a highly motivated and informed workforce who are equipped to implement the necessary safe practices and procedures. These approaches include the following:

- A safety orientation program will inform new employees of their responsibilities and of resources available at NIH.

- Short, practical safety courses or seminars oriented toward specific population needs (laboratory or non-laboratory) will be presented to NIH staff.

- An Occupational Safety and Health Guide and an Environmental Protection Guide will be developed to serve as references for employees.

- A clearinghouse is planned to respond to inquiries on safety-related problems.

Part Two

TRANS-NIH HEALTH PROBLEMS

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Part Two: TRANS-NIH HEALTH PROBLEMS

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INTRODUCTION

TRANS-NIH HEALTH PROBLEMS

Many important diseases, disciplines, research tools, and research resources extend beyond the purview of any single NIH Institute and call for the development of special mechanisms to assure the coordination of efforts within and outside the NIH. In 1977, six such areas of interest which cut across Institute lines were identified for special consideration as "trans-NIH health problems"--Cystic Fibrosis, Diabetes, Arthritis, Genetic Diseases, Nutrition, and Epidemiology. For each of these areas a committee was established to provide a forum for exchange of information, to facilitate collaborative efforts, to coordinate activities within the NIH, and to serve as a point of contact with outside organizations. The committees continue to serve those functions.

During the annual research planning cycle, the Director, NIH, meets with the chairmen and members of selected coordinating committees to review progress, discsuss issues, and assess plans for future activities. The areas selected each year for examination through these special program reviews vary as areas of research mature and new issues emerge which require special attention. When organizational arrangements have been established and are operating effectively to coordinate activities in these cross-cutting areas of special interest the need for formal annual reviews of those topics may be obviated. This constant process of selection assures that special attention is directed only to the most pressing areas of concern and avoids the institutionalization of unnecessary and burdensome formal reporting requirements. The areas not selected for formal review continue to be tended by the appropriate committees, and reporting requirements are satisfied through less formal mechanisms. For instance, a formal program review of cystic fibrosis was not held this year. However, the NIH Cystic Fibrosis Coordinating Committee continues to function as a central integrating focus for cystic fibrosis activities at NIH and serves to stimulate and promote research on all aspects of this health problem through the sponsorship of workshops, conferences and symposia. The Committee also develops joint program announcements to alert the scientific community to areas of research that are of particular interest to the NIH.

This year program reviews were held in four of the original trans-NIH health problem areas--Diabetes, Arthritis, Nutrition, and Epidemiology. In addition, reviews were conducted in three new areas--National Toxicology Program, Research Resources, and Manpower Development.

The following discussion represents the highlights of those meetings.

Chapter 1

DIABETES

TRANS-NIH Diabetes Coordinating Committee

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Chapter 1

SUMMARY OF DIRECTOR'S RESEARCH PLAN REVIEW OF DIABETES

Research Accomplishments

It is encouraging to note the many scientific advancements that have been achieved in the area of diabetes research. These accomplishments occur across the spectrum of research--from fundamental studies of the mechanism by which insulin regulates cellular glucose metabolism, to the development of new techniques for more reliable assessment of the degree to which hyperglycemia is controlled in the diabetic patient, and of improved methods for controlling diabetes.

Among the significant research achievements of the NIH intramural program are included:

- the demonstration that both insulin and insulin receptors are widely distributed with characteristic regional localizations in the central nervous system, providing a basis for extensive regulation by insulin of central nervous system function;

- the demonstration that several common human viruses are capable of inducing diabetes in animal models and producing characteristic changes in human cells grown in culture, and the recent isolation of a virus from the pancreas of a child with acute diabetes which was found to produce diabetes when innoculated into mice;

- the demonstration that insulin stimulates glucose transport in adipose cells by activating a mechanism which translocates glucose transport systems from an intracellular membrane pool to the plasma membrane.

Among the advances supported by NIH funds are included:

- developments in gene isolation, nucleotide sequencing, and recombinant DNA technology which hold great promise for improving understanding of the genetic basis for diabetes, for identifying abnormalities causing various forms of diabetes, and for synthesizing unlimited supplies of insulin;

- accumulation of evidence that point mutations in the proinsulin molecule occur in humans, which may in some instances give rise to diabetic syndromes;

- demonstration that a soluble factor(s) generated in target cells in response to insulin is able to modulate key intracellular enzymes, revealing for the first time a possible intracellular messenger of insulin action;

- new knowledge regarding the etiologies of insulin dependent diabetes, particularly as regards genetic heterogenecity and the role of immunologic and viral factors.

These substantial accomplishments provide exciting prospects for significant future advances in understanding, treating, and preventing diabetes.

Programmatic Accomplishments

It is clear that the NIH Diabetes Coordinating Committee continues to play an active role in the initiation and development of efforts to stimulate and promote research on diabetes and related areas of science. The results of these efforts are rapidly becoming visible. For instance:

- Since the initiation in FY 1977 of the NIH-wide program announcements in diabetes, applications have increased almost threefold.

- The development of the inter-Institute Special Emphasis Research Career Award (SERCA) has resulted in three distinct SERCA programs: (a) cardiovascular aspects of diabetes; (b) obstetrical, perinatal, and pediatric aspects of diabetes; and (c) diabetes and aging.

- The response to the program announcements inviting applications for National Research Service Awards and Research Career Development Awards in diabetes has resulted in a dramatic increase in the numbers of these awards.

- A substantial level of cooperation has been achieved between the NIAMDD and the other NIH Institutes in the support of investigator-initiated research conducted at the Diabetes Research and Training Centers (DRTC) and the Diabetes Endocrinology Research Centers funded by the NIAMDD. In FY 1979, the NIAMDD awarded $7.5 million to support core facilities, pilot and feasibility projects, and information transfer programs. In addition, the NIAMDD awarded approximately $12 million to members of these centers through the support of research project grants. Other NIH Institutes supported regular research grants at these centers at a level of approximately $7 million.

Cooperation has also been achieved between the NIH and outside organizations in the support of diabetes activities. For instance:

- Several Diabetes Research and Training Centers supported by the NIAMDD are developing collaborative programs with the Diabetes Control Program of the Center for Disease Control (CDC).

- The NIH, the National Center for Health Statistics, and private organizations are collaborating, through the auspices of the National Diabetes Data Group, on the analysis of data and the design of future surveys to achieve a more accurate description of the health impact of diabetes.

- The National Eye Institute (NEI), through a cooperative arrangement with the CDC, has transferred funds to the CDC to establish a central laboratory to perform tests in support of the NEI's Early Treatment Diabetic Retinopathy Study.

The National Diabetes Advisory Board

It is especially gratifying to note the cooperation and support that has been evidenced by the National Diabetes Advisory Board. The Board deserves considerable credit for the imaginative and dedicated manner in which it has aided in the development of the diabetes program. That message will be conveyed to the Chairman of the Diabetes Advisory Board.

Resources for the Diabetes Program

The program has adequately met or addressed most of the substantive recommendations of the National Commission on Diabetes. However, the resources available to the program have fallen considerably below the funding levels recommended by the Commission and somewhat below those levels recommended by the National Diabetes Advisory Board.

The manner in which the specific recommendations of the Commission and the Board have been implemented is extremely well documented in the draft report prepared as background for the program review. The draft report will be refined and distributed widely.

In looking at the distribution of current resources according to the Science base, Applications, Technology Transfer, and Training (SATT) model, it is clear that approximately 90 percent of the funds for the diabetes program are devoted to activities in the science base category. This obviously reflects the emphasis the program places on the support of fundamental science in the broad array of disciplines underlying diabetes research. It should be noted, however, that key aspects of the diabetes effort fall under the categories of Applications, Training, and Technology Transfer.

Chapter 2

ARTHRITIS

TRANS-NIH Arthritis Coordinating Committee

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Chapter 2

SUMMARY OF DIRECTOR'S RESEARCH PLAN REVIEW OF ARTHRITIS

It is especially heartening to note the significant research advances that have been achieved in the area of the rheumatic diseases. For instance:

1. Life-saving treatment has recently been developed for the most serious feature of systemic sclerosis (scleroderma), namely, kidney involvement with renal failure and malignant hypertension. Scleroderma has long been considered a poorly understood diffuse connective tissue disease characterized by fibrosis of skin and internal organs. Recent research has shown that the disease seems to be primarily vascular, with arterial lesions in many organs and vasomotor abnormalities. A most prominent early manifestation is Raynaud's phenomenon, during which fingers (and toes) turn white and blue upon exposure to cold or during anxiety. Capillary microscopy of the nailbeds shows attenuation of the microcirculation. Immersing the hands in ice-cold water has been shown to cause vasoconstriction and decreased blood flow in the kidneys and to cause the kidney to produce high levels of renin, leading to hypertension. Cold challenge has also caused shunting of blood in the lungs, followed by pulmonary arterial changes and pulmonary hypertension.

   The leading cause of death in scleroderma is kidney failure with severe hypertension occurring relentlessly and rapidly after it first appears. In the past two years, however, nine patients have been reported to have survived for periods ranging from 1 to 10 years, by aggressive antihypertensive drug therapy, using newly developed agents which: (1) are powerful vasodilators, (2) decrease plasma renin activity, or (3) inhibit the enzyme which converts angiotensin I to angiotensin II. The newly developed agent, Captopril, which acts via the third mechanism has been dramatically effective, bringing the blood pressure rapidly to normal, improving renal function, causing digital ulcers to disappear and even the hardened skin to soften.

2. Research advances are appearing rapidly in systemic lupus erythematosus (SLE), a generalized autoimmune disorder, involving many parts of the body; it is especially serious when it strikes such organs as kidneys, heart or brain. Women are affected 9 times more than men, usually when young, in their childbearing years. A characteristic feature is the large number of both normal and unusual antibodies in the patient's serum: some attack the blood cells, causing anemia; others, such as anti-DNA antibodies combine with DNA as antigen, forming immune complexes which destroy the kidneys; and in the past two years, anti-brain antibodies have been found in SLE patients with

central nervous system disease. SLE tends to run in families: 13 percent of patients have one or more relatives with this disease. Experimental animal models of SLE have been developed in inbred strains of New Zealand mice, especially the B/W strain.

It has recently been shown in both these B/W mice and in patients with SLE that certain types of white blood cells, known as suppressor T-lymphocytes, which normally keep the antibody-producing cells (B-lymphocytes) in check, are defective in SLE. The missing substance in the T-lymphocytes of the B/W mice has been isolated and when this substance is given to young B/W mice, the usual emergence of SLE is impeded.

In addition, the importance of sex hormones in SLE has now been established. In the B/W mice, estrogens (female hormones) accelerate and androgens (male hormones) suppress the expression of SLE, affecting the concentration of anti-DNA antibodies, the extent of immune complex nephritis, and mortality. In addition, last year, abnormal estrogen metabolism has been reported in SLE patients. Women with SLE have elevations of both 16-alpha-hydroxyestrone and estriol; these metabolites of estradiol behave as active estrogens. Accordingly, chronic estrogenic stimulation may well explain the greater prevalence of SLE in women. Of additional interest in this regard is the report that SLE developed in one identical twin, but not in her twin sister who had had her ovaries removed many years earlier. Particularly exciting is a recent study that showed that abnormal suppressor T-lymphocytes were found not only in a majority of patients with SLE, but also in 13 of their healthy first-degree relatives, 12 of whom were women. These findings indicate that both genetic and hormonal factors are modulating autoimmunity before either clinical symptoms or autoantibodies appear. Scientists, therefore, are now provided with exciting opportunities to make rapid progress in understanding the cause of this important and baffling disease, and to devise new precise forms of treatment, such as replacing the deficient lymphocyte substance or correcting the sex hormonal inbalance.

3. Lyme arthritis, which first appeared as a medical curiosity in a mid-coastal area of Connecticut three years ago, has become a disease of considerable interest in its own right and is also providing important information on mechanisms by which chronic arthritis develops in a disease of presumed infectious etiology. Lyme arthritis begins after the bite of a tick, now identified as the species, Ixodes Scapularis, with a spreading skin lesion followed by acute arthritis. Clusters of cases have also been found on Cape Cod and in Wisconsin. The original series has now grown to over 200; several patients have developed a chronic arthritis, with overgrowth of inflamed synovium (pannus formation) and cartilage erosion, closely resembling rheumatoid arthritis. Immune complexes (identified as IgM cryoglobulins) have been demonstrated in the patients' serum early in the disease, and in the synovial fluid later in the disease in those developing chronic arthritis. A genetic determinant seems to be operative since

it has been shown recently that those with chronic arthritis have a high incidence of the histocompatibility antigen DRW2.

Thus, Lyme arthritis mimics rheumatoid arthritis in several ways. These interesting findings should encourage investigators of rheumatoid arthritis to accelerate the search for a causative infectious agent. A candidate agent has, in fact, been recently identified: antibodies to EB-viral-antigen have been demonstrated in both serum and synovial fluids of patients with rheumatoid arthritis, and seem to be related to disease activity. Genetic susceptibility is also important in rheumatoid arthritis. However, the HLA specificity in rheumatoid arthritis seems to be due to another tissue antigen, DRW4, which has been shown to be present in 52 percent of patients compared to 8 percent in controls.

4. Scientists have now revealed evidence of molecular modulation of the immune response. For over a decade, specific enzyme deficiencies have been known to be associated with gout, usually in severe forms in young people. Now, three such enzyme deficiencies in purine catabolism have been discovered to be associated with severe clinical immunodeficiency states leading to death in children. Deficiencies of two of these enzymes cause the accumulation of metabolic products (ATP and GTP) which in turn leads to dysfunction of T-lymphocytes. Congenital agammaglobulinemia has been found to be associated with deficiency in the enzyme, lymphocyte ecto-5-nucleotidase. Incidentally, a deficiency of one of these three enzymes (PNP) has been found in the T-lymphocytes of patients with systemic lupus erythematosus (SLE). Thus, serious immunologic diseases can now be expressed in biochemical terms, offering the hope of similar discoveries in other immunologic diseases, and opportunities for therapeutic replacement.

National Arthritis Advisory Board

The National Arthritis Advisory Board was established in 1977 to review and evaluate the implementation of the National Arthritis Plan and to recommend to the Congress, the Secretary, and the heads of appropriate Federal agencies with respect to the Arthritis program.

The Board has served a useful function in providing an oversight of arthritis related activities conducted along the spectrum from basic research to the delivery of health services. And it also has provided a valuable service in facilitating interaction among the Federal agencies and private organizations which share an interest and responsibility in arthritis.

The Board, funded at an annual level of approximately $300,000, meets four times a year in regularly scheduled sessions and also convenes a variety of special conferences, workshops, and symposia to stimulate and promote activities in the area of arthritis.

In keeping with a general move to reduce the operating costs of doing business at the NIH, ways will be sought to streamline the operations of the Board without impairing its effectiveness.

Arthritis Interagency Coordinating Committee

The Arthritis Interagency Coordinating Committee, created by the National Arthritis Act of 1974, is functioning effectively through the use of special subcommittees. For instance:

- The Epidemiology Subcommittee is directing the development of an annotated bibliography on the epidemiology of the rheumatic diseases. It will review the literature since 1966 when the last in-depth review, "Population Studies of the Rheumatic Diseases," was published. A national workshop on rheumatic diseases epidemiology is scheduled for September, 1980.

- A Data Systems Subcommittee was formed in 1979 to review ongoing data collection systems and evaluate national data on arthritis and related diseases. The initial meeting of the Subcommittee was devoted to an examination of data banks such as the coronary artery disease bank at Duke and the arthritis data bank, ARAMIS, at Stanford; and the next meeting will address issues relating to statistics in the rheumatic diseases.

NIH Arthritis Coordinating Committee

During last year's program review of arthritis it was agreed that the NIH Arthritis Coordinating Committee should be viewed as a research subcommittee of the Arthritis Interagency Coordinating Committee. It appears that this arrangement is working exceptionally well and should be continued. The activities of the NIH Arthritis Coordinating Committee have served to complement the work of the Interagency Committee. Among those activities are included:

- A productive conference on collagen metabolism was held at NIH, under the joint sponsorship of NIAMDD and NIDR, to identify future directions for research on osteogenesis imperfecta. Recent evidence was presented concerning the genetic control of specific types of collagen, and discussion centered on the correlation of genetic classification of osteogenesis imperfecta with biochemical and histopathologic abnormalities of collagen and bone.

- A conference is planned on immunogenetics and the potential relationship of bacterial and viral infections to rheumatic diseases. The proposed conference is aimed at fostering research on mechanisms whereby histocompatibility antigens influence susceptibility to disease and on identifying environmental factors that initiate disease.

- A workshop will be co-sponsored by NIAMDD and NINCDS, in association with the Committee of Research of the American Academy of Orthopedic Surgeons, on "Research Strategies on the Pathogenesis of Back Diseases" with emphasis on the extremely common idiopathic forms of back disease.

Multipurpose Arthritis Centers

The NIAMDD provides support to 24 Multipurpose Arthritis Centers for the conduct of (a) basic and clerical research, (b) professional, patient, and public education programs, and (c) community-based demonstration programs. These centers were funded at a total level of $6.2 million in FY 1979. It is anticipated that approximately 26 centers will be funded in FY 1980 and FY 1981.

In FY 1980, 15 of the centers will be reviewed for renewal. The results of the peer review of these competing renewals will condition the general funding strategy for this center grants program.

Chapter 3

NUTRITION

TRANS-NIH Nutrition Coordinating Committee

Chairperson:

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Chapter 3

SUMMARY OF DIRECTOR'S RESEARCH PLAN REVIEW OF NUTRITION

Clinical Nutrition Research Units

Four Clinical Nutrition Research Units (CNRUs) have been established to provide a focal point for clinical nutrition research at medical schools and other institutions conducting biomedical research. These four units (three supported by NIAMDD and one by NCI) were funded at a total level of $1 million in FY 1979, and it is anticipated that an additional six to eight such units will be funded in FY 1980.

NIH Nutrition Newsletter

Approval is being sought to initiate publication of a Nutrition Newsletter intended for distribution to NIH grantees, members of the National Nutrition Consortium, Federal agencies, medical schools, private foundations, and others. The Newsletter will contain (a) a feature column written by the Director, NIH; (b) progress reports on nutrition research; (c) a list of program announcements; (d) notifications of nutrition conferences, workshops, and symposia; (e) a list of funded research grants, contracts, training grants, and fellowships; and (f) other items of interest to nutrition professionals.

The Office of Management and Budget (OMB) has withheld approval of the Nutrition Newsletter and has requested information concerning the need for the Newsletter and why it should be an NIH publication rather than a joint NIH-USDA effort. In response, a memorandum will be sent by the Secretary, HEW, to OMB which describes the purposes of the proposed Newsletter and establishes the need for HEW to develop such a publication. The focus of the publication will extend beyond the interest and activities of the NIH to encompass the broad nutrition research activities of the Department.

Conferences, Workshops, and Symposia

The Committee remains active in stimulating research and advancing the synthesis of knowledge in nutrition through the planning, conduct, and support of a variety of meetings. For instance:

- A workshop, "Nutritional Support of the Patient: Research Directions for the 1980s," was held in September 1979, and included participants from national and international scientific institutions. The proceedings of the workshop will be published in a special supplement of the American Journal of Clinical Nutrition. The workshop was quite successful and the recommendations growing from this meeting should provide a basis for pursuing additional research approaches through the development of program announcements and RFAs.

- A three-day International Conference on Nutritional Status is planned for April or May of 1980. The meeting will be sponsored jointly by the NIH, FDA, CDC, and NCHS.

In addition to maintaining support of traditional conferences and workshops, the NCC will examine the wide array of questions concerning the role of nutrition in health and select for special consideration those topics that might be amenable to clarification, or perhaps resolution, through the conduct of consensus development activities. The Committee will work very closely with the Office of Medical Applications of Research, NIH, in selecting appropriate topics for consensus activities.

Computerized Data Retrieval System

The NCC has developed an operational definition of nutrition research, prepared a set of descriptors, and organized a manual data retrieval system for the reporting of reliable data on nutrition and nutrition-related research. The Committee is working with the Division of Computer Research and Technology (DCRT) to convert the manual system to a computerized system which will facilitate the preparation of annual reports and decrease the time and effort required in responding to a variety of queries.

Nutrition Education

The NCC's Subcommittee on Nutrition Education conducted a critical review of all nutrition publications developed at the NIH for purposes of public and professional education. This was an extremely valuable contribution, and the Subcommittee will maintain this function as a continuing responsibility.

A large supermarket chain has asked the NCC to participate in a consumer education program. The NCC will assist by (a) identifying topics in nutrition that represent appropriate subject matter for inclusion in publications such as consumer almanacs, and (b) developing literature on selected topics. The supermarket will support the costs of printing and distributing the material. (The literature will be made available to the general public and will not be limited to customers of this particular food chain.)

Program Announcements

The NCC has been effective in promoting research through the development of joint program announcements, requests for applications (RFAs) and requests for proposals (RFPs). The Committee will continue to stimulate nutrition research through (1) the development of a program announcement or request for application in the area of parenteral and enteral nutrition; (2) the reissuance of a program announcement on obesity; and (3) the development of a program announcement on behavior and nutrition.

Chapter 4

EPIDEMIOLOGY

TRANS-NIH Epidemiology Committee

Chairman:

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Chapter 4

SUMMARY OF DIRECTOR'S RESEARCH PLAN REVIEW OF EPIDEMIOLOGY

Since its establishment in 1977, the NIH Epidemiology Committee has provided a useful forum for discussion of issues of concern to epidemiologists in all the Institutes and has served as a central focus for interaction with other agencies on matters concerning epidemiology.

Legislation Governing the Use of Medical Records

The Committee has assisted the legislative liaison offices of the NIH and the Department in assessing the potential impact on epidemiologic research of several legislative proposals that have been introduced governing the use of medical records. The Committee has also provided information that was useful in the drafting of the Administration's medical record privacy bill. The current draft of the Administration's bill to protect medical records provides strong measures to guard against abuses of medical information although it recognizes the importance of continuing to provide biomedical investigators direct access to these data in order to satisfy legitimate research needs.

Freedom of Information Act

It appears that the Freedom of Information Act has created a set of circumstances that could serve as a constraint on the conduct of epidemiologic research. Under the provisions of the Freedom of Information Act, epidemiological data collected by investigators through long and arduous efforts must be released to anyone requesting those data. Such data must be released before they have been refined and analyzed and before the originators of these data have had the opportunity to publish in professional journals the results of analytic studies based on the data. These circumstances constitute a strong disincentive to investigators to expend their professional time and effort in the task of collecting primary epidemiologic data. And since the collection of such "raw" data forms the foundation of epidemiologic research, this legislation could have a serious disruptive effect on the field of epidemiology.

Reduction of Reporting Burden

The Office of Management and Budget has issued a Notice of Proposed Rulemaking to introduce regulations intended to reduce the burden of reporting time imposed by Federal agencies. The proposed regulations would establish for each agency a ceiling on the total number of hours of response time that may be required of respondents by that agency to fulfill its information needs. Reporting time expended in response to NIH forms designed to collect epidemiologic data would be included under the NIH ceiling. Under the conditions of

this regulation, an agency that reaches its ceiling would be required to request from the OMB an extension of its allotted reporting response time before any additional reporting requests could be made by that agency.

The proposed regulation would pertain not only to that reporting time required in response to agency-initiated requests but would extend to include voluntary response time generated in the preparation of unsolicited documents received by the agency. This would mean, for instance, that the reporting time required by applicants in developing research and training grant applications would be counted against the NIH ceiling.

It is clear that this proposal would have a serious adverse effect on the research programs of the NIH. The circumstances warrant an exemption of certain NIH programs from the full provisions of this proposed regulation. Toward this end the Committee will develop a draft issue paper that describes the nature of the proposed regulation and discusses the potential effect that such a regulation would have on the NIH programs.

PHS Training Program in Epidemiology

It is especially pleasing to note the progress that has been made in developing a PHS training program in epidemiology. Up to fifteen persons per year will be accepted as commissioned officers in the Public Health Service for a three-year period of duty. During the first year, each successful applicant will attend a university of his or her choice, at government expense, as a candidate for the M.P.H. or equivalent degree. During the subsequent two years, trainees will work in association with senior epidemiologists in the participating PHS agencies. A matching procedure will be employed to assure that each trainee is assigned to a preceptor whose area of expertise is of interest to the trainee.

Approximately 50 applications were received in response to the initial program announcement, and from this group a maximum of thirteen persons will be selected for the first class. The recruiting schedule will be adjusted next year to coincide better with the academic calendar and thus provide an added recruitment advantage.

Chapter 5

RESEARCH TRAINING AND MANPOWER DEVELOPMENT

TRANS-NIH Committee on Research Training
and Manpower Development

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Chapter 5

SUMMARY OF DIRECTOR'S RESEARCH PLAN REVIEW OF MANPOWER DEVELOPMENT

The discussion of manpower development was enriched greatly by the participation of Dr. Bondurant and Mrs. Wexler of the NIH Director's Advisory Committee (DAC), and Dr. Tosteson, consultant to the DAC.

In January, 1979, the Coordinating Committee on Manpower Development was established to assess the current NIH training policies and procedures and to recommend modifications, where necessary, to achieve a cohesive NIH approach to assuring the availability of an adequate number of biomedical and behavioral research personnel to carry out the missions of the Institutes. It is clear that the mandate of the Committee extends well beyond the realm of "training" or "manpower development" per se and includes responsibility for activities concerned with the deployment and effective utilization of trained research personnel. Accordingly, the name of the Committee will be changed to the "Committee for Research Manpower" to more accurately reflect the Committee's true mandate.

In view of the difficulty of the tasks implicit in the mandate of the CCMD, the Committee has accomplished a great deal in the relatively short span of one year. For instance:

1. After much deliberation, the decision was made to (a) increase stipends to a level more competitive with other forms of remuneration in an effort to continue to attract individuals into biomedical research careers, and (b) adjust institutional allowances for training grants and fellowships made under the National Research Service Award (NRSA) authority in order to relate institutional allowances directly to the number of individuals being trained and to permit the separation of stipend levels from the calculation of institutional allowance in any future adjustments.

2. The CCMD examined the recommendations made by earlier committees working within the NIH on problems related to manpower development and selected for implementation a recommendation to establish a Senior Fellowship Award which offers established investigators the opportunity to develop new skills within their areas of research competance or to expand into additional areas of research. Authority to establish the program was obtained when a special exception to the stipend ceiling which exists under the NRSA authority was granted to accommodate the senior status of these fellows.

3. Guidelines and program announcements were developed by the Committee for a program which provides short-term research training to students who are seeking professional degrees in medicine, osteopathy, dentistry, veterinary medicine, optometry, pharmacy, and podiatry. The awards, offered for periods of up to three months per year, are designed to provide a research exposure to students during the early

stages of their professional development with the aim of attracting these individuals to careers in clinical investigation. The premise and concept of this program is sound and the continuation and expansion of this mechanism should be encouraged. However, the bulk and complexity of the application forms for this program place an onerous administrative burden on the participating universities. This concern was expressed also by the representatives of the DAC. The Committee will seek the participation of university representatives in distilling and refining the application forms and procedures and minimizing the overall burden of participation in this program.

4. The CCMD has been successful in consolidating the many diverse forms of NIH support for new and young investigators into a single, uniform NIH support mechanism--the New Investigator Research Award (NIRA). This program, which provides research support for periods up to three years, is designed to help new investigators make the transition from training status to that of established investigator, and to aid those established investigators who wish to change their field of scientific activity. A similar effort will be undertaken by the Committee to codify the diverse manpower development mechanisms that exist to attract clinicians into research careers and foster their professional development.

5. In an effort to improve the NIH system for characterizing the areas of predoctoral training supported under training grant awards, the Committee examined the huge array of disciplines, fields, specialties, sub-specialties and diseases used previously to classify the areas of training and compressed and modified these into 12 major categories. This new classification system--which will be used to display the distribution of trainees, by supporting Institute, according to the 12 major categories of training--should prove to be a valuable aid in charting the progress of our current training efforts, assessing our future needs, and planning new training strategies.

6. The Committee reviewed a study which was conducted to (a) determine the extent to which recipients of National Research Service Awards (NRSA's) perform acceptable services to satisfy the payback requirements of these awards; and (b) characterize the nature of such services. The results of that analysis revealed that more than 99 percent of NRSA recipients chose to perform services as a means of paying back the costs of their awards. Approximately 85 percent of these recipients served as faculty members and staff at universities and medical centers; another 8 percent engaged in acceptable activities in industry; and nearly 7 percent chose appropriate service in government. Overall, it is clear that the initial NIH experience with the NRSA has indeed been satisfactory.

It appears that the Committee has an ambitious agenda of ongoing and future activities.

1. Plans are being considered for the possible development of a program to provide part-time research training to individuals who, for a variety of valid reasons, cannot engage in such activities on a full-time basis. The discussion underscored the need to assess the desirability and feasibility of providing additional training opportunities and at the same time guard against the development of programs that will provide superficial training experiences which will not be adequate to prepare an individual to compete sucessfully in a rigorous and intense research environment.

   The National Science Foundation (NSF) has initiated a program of part-time research training which will be followed closely by the Committee in an effort to apply the knowledge gained from the NSF experience in deciding upon the advisability of undertaking an NIH pilot program.

2. Perhaps the most important task facing the Committee in the near future is the consideration of how to shape the future training programs of the NIH in ways that will assure the continued capability to meet national research manpower needs. Clearly, the institutional training grant award provides an important control on the quality of training supported by the NIH and permits adjustment of training environments to meet perceived changes in training needs. However, with the prospect of repeated attacks upon institutional support mechanisms looming large, it becomes incumbent upon us to devise effective alternatives to the institutional training grant award. It is clear that the continued health of the research enterprise is critically dependent upon the availability of high quality research training. This is a task to which we must all devote considerable energy.

Chapter 6

MAINTENANCE OF RESEARCH RESOURCES

TRANS-NIH Research Resources Coordinating Committee

Chairman:

Dr. William F. Raub
Office of the Director
National Institutes of Health
Building 1, Room 107
Bethesda, Maryland 20205

Executive Secretary:

Mr. C. Alan Moore
DRR
Building 31, Room 5B05
Bethesda, Maryland 20205

Chapter 6

SUMMARY OF DIRECTOR'S RESEARCH PLAN REVIEW OF RESEARCH RESOURCES

The Research Resources Coordinating Committee was established to provide advice in planning more effectively the development and stabilization of both general and categorical shared extramural research resources. To accomplish this goal the Committee will (a) review the shared research resources now supported by the Division of Research Resources (DRR) and the Institutes; (b) recommend changes in the current programs where appropriate to meet NIH's needs in the most scientifically productive and economical ways; (c) assess the adequacy and appropriateness of long-range plans developed by the DRR and the Institutes for the development and use of research resources; (d) identify performance indicators which can be used to measure the impact of shared research resources and evaluate the contributions that these resource programs have made to the NIH mission; and (e) provide advice to the Director, NIH, and appropriate National Advisory Boards and Councils regarding plans for the future development of shared research resources.

It is clear that the work of the Committee will be especially useful as we progress in our effort to identify the problems besetting research institutions and initiate actions to stabilize the research environment.

Impact of the Biotechnology Research Program

The Committee conducted a pilot study as part of an effort to assess the degree to which the resources made available through the Biotechnology Resources Program have contributed to the progress of research projects funded by the NIH. A questionnaire was developed by the Committee and sent to a sample of NIGMS staff. Information was requested which would permit a determination of the contributions made to the research of NIGMS-funded investigators by the shared research resources provided through this program. The questionnaire focused specifically on the usefulness of the computer resources, high voltage electron microscopy, fast reaction kinetics, nuclear magnetic resonance/ electron spin resonance, mass spectrometry, and stable isotope compounds that have been made available to these investigators.

The results of this preliminary survey indicate that the respondents believe very strongly that the research resources provided by this program have indeed aided them substantially in the conduct of their research. The Committee will examine further the design and preliminary results of this pilot study and determine if it would be useful and productive to expand the study to include a sample of extramural staff from each of the Institutes.

Future Activities of the Committee

The Committee has developed a substantial list of topics and issues which deserve attention during the next several years. These subjects include:

1. Instrumentation

A variety of mechanisms exist at the NIH for developing and making available on a shared basis highly innovative instruments and technologies for application to biomedical research. The Biotechnology Resources Program in the Division of Research Resources provides investigators access to a wide range of computer systems, specialized equipment for the study of the structure and function of complex biological systems, and unique cellular and biochemical materials. In addition, many of the Institutes provide core grants and special instrumentation awards which include support for the cost of moderately priced equipment to be shared by investigators at the recipient institutions.

The Committee will examine the current array of mechanisms for the support of shared instrumentation in an effort to determine the adequacy and appropriateness of this mix and to identify ways in which a more cohesive and effective NIH program might be developed.

2. Facilities for Clinical Research

The Clinical Research Program of the Division of Research Resources supports General Clinical Research Centers (GCRCs) which serve as institutional resources for clinical research and clinical training. These clinical research centers provide an environment for the conduct of clinical investigations across the full spectrum of disease entities. The vast majority of the research conducted in the centers is supported under research grants funded by the various NIH Institutes. Consequently, a range of possibilities exists for collaborative arrangements between the DRR and the categorical Institutes. The Committee will explore the role it might play in coordinating interaction between the DRR and the Institutes to achieve the optimal utilization of this important resource and to increase the effectiveness and efficiency of the NIH clinical research programs.

3. Other Research Resources

For many years the NIH has supported the development and care of various specialized animal colonies, and the maintenance of collections of microorganisms and cell lines. Historically, the responsibility for the management and funding of these resources has been fragmented and uneven. The Committee will address this chronic issue in an effort to develop a more uniform policy concerning the most appropriate organizational arrangements and funding sources for the support of these resources.

A similar effort will be made to develop a more systematic approach to the maintenance of specialized information systems and data bases for which we have no adequate institutionalized systems of support (e.g., the NIH/EPA Chemical Information System).

Chapter 7

NATIONAL TOXICOLOGY PROGRAM

TRANS-NIH National Toxicology Program

Chairman:

Dr. David P. Rall
NIEHS
P. O. Box 12233
Research Triangle Park, North Carolina 27709

Contact:

Mr. George M. Kingman
NIEHS
P. O. Box 12233
Research Triangle Park, North Carolina 27709

Chapter 7

SUMMARY OF DIRECTOR'S RESEARCH PLAN REVIEW OF THE NATIONAL TOXICOLOGY PROGRAM

Purpose and Goals of the National Toxicology Program

The National Toxicology Program (NTP) was established by the Secretary, HEW, on November 15, 1978, for the purpose of strengthening the Department's activities related to the testing of chemicals of public health concern and the development and validation of new and better integrated test methods.

The goal of the program is to integrate the toxicology research and testing activities of the relevant HEW research agencies in order to strengthen the science base underlying toxicology testing and to better provide needed information to regulatory agencies. The program is designed to: (1) broaden the toxicological characterization of chemicals being tested in order to study the full range of potential human health effects; (2) increase the rate of chemical testing so that chemicals most likely to cause human harm may be determined quickly; and (3) develop and validate a series of testing protocols which will permit regulatory actions to be based on more detailed scientific information and allow a greater focus on those chemicals which actually need some type of control.

The program is comprised of the relevant activities of the Food and Drug Administration (FDA), the Center for Disease Control/National Institute for Occupational Safety and Health (CDC/NIOSH), the National Cancer Institute (NCI), and the National Institute of Environmental Health Sciences (NIEHS).

Annual Plan

The Secretary has approved the second NTP annual plan. The plan includes (1) a review of current HEW research in toxicology; (2) a description of program activities to be undertaken by the NTP; (3) a list of compounds to be tested and test procedures to be followed; (4) a discussion of the regulatory and scientific opportunities considered in the development of the plan; (5) a schedule for the accomplishment of the tasks described in the plan; and (6) a discussion of the resources required to implement the plan.

An announcement will be placed in the Federal Register to notify the public of the availability of the plan.

Board of Scientific Counselors

The NTP is in the process of establishing a Board of Scientific Counselors composed of non-governmental scientists to provide advice on scientific program content and policy issues. One immediate function of the Board will be to participate in the development of a process by which information generated by the program can be most effectively processed, reviewed, synthesized, and ultimately released to appropriate agencies and to the public.

With regard to the carcinogenesis testing program, the role proposed for the new Board is similar in some respects to that which is currently exercised by the NCI Clearinghouse for Environmental Carcinogens. We should determine now the appropriate role of the new Board vis a vis the NCI Clearinghouse to avoid undue confusion and to prevent potential duplication of effort.

Annual List of Potential Carcinogens

The NTP, in accordance with Sec. 262, PL 95-622 (the McGuire Amendments), is responsible for preparing and publishing annually: (1) a list of substances known or suspected to be carcinogenic in humans; (2) information concerning the numbers of individuals exposed to such substances and the nature and level of those exposures; and (3) an evaluation of the current regulation of such substances, including an assessment of the extent to which regulation reduces human risk.

A list of known or potential carcinogens has been distributed to the various regulatory agencies with the aim of enlisting their aid in estimating the levels of exposure to these substances and assessing the adequacy of current standards for the regulation of these compounds. However, a great deal remains to be done in order to improve the capability to carry out these assessments.

Broadening of Toxicology Testing

A major portion of the current resources of the NTP is devoted to the performance of lifetime carcinogenicity bioassays. Activities will continue to focus on the improvement of carcinogenic bioassays, the development of less expensive and more rapid methods that may, at least partially, obviate the need for lifetime animal tests, the study of the relationship of chemical structure of compounds to biological activity, and the development of tests to study the effects of combination of chemicals.

Clearly, an important goal of the NTP is to broaden the toxicologic characterization of chemicals to include emphasis on: (1) establishing the feasibility, relevance, and validity of behavioral testing procedures for measuring and predicting the effects of chemical insults on the nervous system; (2) determining the utility of current test methods for predicting the likelihood that a chemical will cause developmental defects in humans, and screening selected chemicals to assess reproductive and developmental effects; (3) fostering the integration of genetic end points with those of other longand short-term toxicology tests; and (4) developing improved tests to detect early biochemical, immunologic, or physiologic abnormalities associated with the development of pulmonary diseases.

The rate of expansion in these additional areas of toxicology will depend upon the amount of resources available to the program.

International Cooperation

It is encouraging to note that the NTP is forging important links with its counterparts in other countries. The NTP will work with the World Health Organization (WHO) to develop a mechanism for the peer review of technical monographs on selected chemicals. Through such a mechanism, the results of studies evaluating the health effects of specific chemicals will be readily available throughout the world.

The NTP is also supporting and participating in an international collaborative study, under the auspices of the International Association of Environmental Mutagen Societies, to evaluate a range of mutagenicity assay systems for their ability to predict chemical carcinogenicity.

Resources Required by the NTP

In view of the uncertainty surrounding the level of resources that will be made available to the NTP, it is necessary at this time to consider the possible effects on the program that might be anticipated under varying levels of resources. A discussion paper should be prepared that describes your views of the consequences that would obtain under each of the following assumptions:

1. FY 1980--increase in funds but no increase in position ceilings.

2. FY 1981--increase in funds but no new positions.

Future of NTP

Our discussion called attention to the fact that the NTP was established as an experimental program and, as such, is subject to review and assessment by the Office of the Secretary in approximately one year. It is clear that the current organizational arrangement does not provide the stability that is necessary for long-range planning and sound program development. It is important for us to meet soon to begin considering the options available for the future development of the NTP.

To aid us in our deliberations on the future course of the NTP, it will be necessary to develop a discussion paper that (1) outlines briefly the current organizational structure of the NTP, (2) describes the shortcomings created by the existing organizational arrangement, (3) suggests new organizational arrangements which would provide an appropriate corporate structure for the continued development of the NTP, and (4) describes the actions that would be necessary to implement the proposed organizational arrangements.

APPENDICES

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APPENDIX A

MEMORANDUM

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTE OF HEALTH

O : B/I/D Directors

DATE: September 11, 1979

ROM : Associate Director for
Program Planning and Evaluation

UBJECT: Guidance for Development of the NIH Research Plan, FY 1982-84

Attached are the following documents:

- A draft outline of the FY 1982-84 NIH Research Plan and a listing of OD program planning and financial management staff responsible for development and coordination. (Attachment I, p. 1)
- Guidance for the development of B/I/D Research Plan submissions. (Attachment II, pp. 2-15)
- A schedule for the development and review of the NIH Research Plan. (Attachment III, p. 16)
- A listing of OD staff responsible for the initial review of the B/I/D submissions. (Attachment IV, pp. 17-18)
- A schedule for the Director's Review Sessions. (Attachment V, p. 19)

As you can see from the guidance, both the content and the process governing the Research Plan are very similar to that of last year. One additional trans-NIH health problem has been identified by Dr. Fredrickson for inclusion in this year's planning process, namely, the NIH component of the National Toxicology Program; while two included in last year's process have been discontinued, Genetics and Cystic Fibrosis. The status of the current trans-NIH health problems (Diabetes, Arthritis, Nutrition, Epidemiology and the National Toxicology Program) will be reviewed. Guidance for reporting on the status of these will be forwarded to the committee chairperson soon.

In addition, two areas of special concern have been identified by Dr. Fredrickson and will be included in this process. These are the Maintenance of Research Resources and Research Training and Manpower Development. Each of these already have established committees composed of OD and BID staff reviewing issues which exist in these areas. A review session has been scheduled with these two committees to address these areas of special concern.

This year's Director's review sessions will focus heavily on our efforts to develop further an approach for stabilizing research project grants over the next five years. This issue will be examined under rigorous budget assumptions, and will include an analysis of the impact stabilization could have on an Institute's total range of activities. Bill Raub has assembled a work group which has been addressing this problem for several months now. Dr. Fredrickson has asked them to extend their work from a collective NIH approach to an individual Institute approach during September and October. They will be working closely with each Institute during this time, and you may expect some notice and guidance to this effect soon. By the time the review sessions begin in mid-November, much analytical work will have been accomplished so that the review sessions can begin from a common framework and quickly focus on key problems that must be addressed.

I look forward to a productive exchange as we proceed through this planning process. Please submit 30 copies of all material requested in a single package to Kurt Habel, Building 1, Room 205, by November 1. Also submit at that time a list of B/I/D participants (name and title) in the Director's Review sessions, as well as a list of issues which may arise at the appropriations hearings and should be placed on the agenda. Guidance for the development of legislative proposals will be forwarded as soon as it is prepared and will be integrated into the planning process as in past years.

Joseph G. Perpich, M.D., J.D.

Attachments

cc:
B/I/D Planning Officers
B/I/D Budget Officers
B/I/D Legislative Contacts
OD Staff
Deputy Assistant Secretary for
  Health Planning and Evaluation, H
PPE Directors
Mr. Mansfield
Mr. Miller
Chairperson, Trans-NIH Committees

Attachment I

DRAFT OUTLINE OF NEXT YEAR'S RESEARCH PLAN

I.	NIH Director's Overview	Kurt Habel, DPA 496-1454
II.	NIH Budget Proposal, FY 1982	Dick Miller, DFM 496-4477
III.	NIH Institute and Research Plans (will include: a. Director's Overview Statement b. 1981 Program Changes c. 1982 Program Changes)	Kurt Habel, DPA 496-1454
IV.	Director's Review Sessions (Memorandum of understanding to be edited by OD Program Planning Branch staff and reviewed by B/I/D staff prior to inclusion)	Kurt Habel, DPA 496-1454
V.	Trans-NIH Health Problems	Ed Lynch, DPA 496-1454
VI.	Legislative Plan	Burke Zimmerman, DLA 496-3471

Attachment II

CONTENT OF B/I/D RESEARCH PLAN SUBMISSIONS FOR 1982

I. Format for Bureaus, Institutes, Research and Service Divisions (DRR, DRS, DCRT, CC) Submissions--due November 1, 1979.

A. Director's Overview Statement (3 double-spaced pages)

1. Brief statement on significance of the health problem.

2. Statement on research program strategy developed to deal with health problem.

3. Goals--relevance of research program strategy to broader health objectives, such as prevention of disease and the containment of health care costs.

B. FY 1981 Program Changes (4 double-spaced pages)

(Note: The intent here is not to address each research program, but to focus only on major program changes necessitated by the FY 1981 budget process.)

1. Highlight major activities that will be initiated in FY 1981, as a result of the 1981 budget process.

2. Highlight major initiatives that will be maintained in FY 1981, as a result of the 1981 budget process.

3. Highlight major initiatives that must be cut back, eliminated, or not started in FY 1981 as a result of the 1981 budget process and that the B/I/D feels strongly should be restored.

4. Brief discussion of directives resulting from FY 1980 Appropriations Committee Reports and their impact upon FY 1981 Plans.

C. FY 1982 Program Changes (4 double-spaced pages)

(Note: The intent here is not to address each research program, but to focus only on major program changes planned above the 1982 Current Services level.)

1. Major program changes planned for 1982. Should include new initiatives, expansion of ongoing activities, shift in emphasis and cut-backs in programs, including training programs and other resource programs (excluding on-campus buildings and facilities).

2. Potential impact of program changes on three year period (1982-84). (For example, if a B/I/D plans to initiate a center program in a research area in 1982, what will be the proposed scope and estimated budget of such a program by 1984?)

D. B/I/D Budget Section

(See attached budget tables. Although only highly aggregated budget data will be presented in the final Forward Plan, the data requested here is necessary for review purposes and routine budget process requirements. Budget submissions for the Central Service Divisions will be handled separately, as they were last year.)

II. Director's Review Sessions.

(Agendas to be developed jointly by B/I/D's and OD, NIH.)

A. Sessions will focus on the stabilization of research project grants during period 1981-1985, and the impact this approach may have on other program activities.

B. Sessions will focus on 1981 and 1982 program changes and priorities.

C. Sessions will focus on Science base (S), clinical Applications (A), Transfer (T), and Training (T) approach.

D. Sessions will focus on selected problems and issues which may arise at Appropriations Hearings.

E. Sessions will focus on follow-up of major issues identified in last year's Director's Review sessions.

September 10, 1979

Instructions for Budget Tables

The following tables are required for the 1982 Research and Legislative Plan:

1. SATT for 1980 to 1984
2. Research Programs for 1980 to 1982
3. Mechanism for 1980 to 1982
4. Crosswalk of SATT to Mechanism for 1980 to 1982
5. Calculation of the 1982 Current Level
6. Funded - Unfunded Analysis for 1980 to 1982
7. Training Analysis for 1980 to 1982

The 1980 Planning Assumption should reflect the 1980 column of the 1981 OMB submission.

The 1981 Planning Assumption should reflect the 1981 column of the 1981 OMB submission plus an estimate for the October 1980 pay raise at 7%.

The 1982 Current Level is the 1981 Planning Assumption plus administrative mandatory increases. No pay raise may be anticipated for October 1981. FECF and FTS increases for 1982 will be provided to Financial Management Officers and Budget Officers under separate cover. Within the total dollar level for 1982, funds may be distributed among mechanisms and programs as desired.

Additional instructions for Central Services divisions will be provided under separate cover.

APPENDIX B

MEMORANDUM

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH

TO : B/I/D Directors

DATE: October 31, 1979

FROM : Director, NIH

SUBJECT: Stabilization of the Science Base--the Director's Program Review Sessions

Stabilization of the science base has been proposed as a major initiative in the HEW Health Research Planning Process - Phase II and has been the subject of much work by a subcommittee of BID Directors. As part of the Director's Program Review Sessions this fall we will discuss the promise and problems of the stabilization initiative as it may affect each BID. Specifically, my staff and I need to know how each BID would attempt to stabilize the science base in general--and research project grants in particular--for each of three possible total BID budgets for the FY 1982-84 period:

1. fixed level for all three years at the FY 1981 planning assumption,

2. a BID level increasing at the rate of 8 percent per year starting from the FY 1981 planning assumption, and

3. a BID level increasing from the FY 1981 planning assumption in accordance with your professional judgment.

In preparing the required budget data, an 8 percent inflation rate for 1982, 1983 and 1984 should be used.

To facilitate review and discussion of this aspect of your Research Plan, we would appreciate having, for each of the three levels, a 1-page summary of your proposed approach to stabilizing the science base and a standard mechanism budget table (format attached). Thirty copies of this material should be submitted to Kurt Habel, Building 1, Room 205, ten calendar days before your scheduled Research Plan Review Session.

I appreciate your cooperation in developing this information in addition to that requested in Dr. Perpich's memorandum of September 11.

Donald S. Fredrickson, M.D.

Enclosure

cc:
B/I/D Planning Officers
B/I/D Budget Officers
OD Staff
PPE Directors
Mr. Mansfield
Mr. Miller

APPENDIX C

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

NATIONAL INSTITUTES OF HEALTH

List of Witnesses

Dr. Donald S. Fredrickson, Director, National Institutes of Health

accompanied by

Dr. Thomas E. Malone, Deputy Director, National Institutes of Health

Leon M. Schwartz, Associate Director for Administration, National Institutes of Health

Norman D. Mansfield, Director, Division of Financial Management

and

Wilford J. Forbush, Deputy Assistant Secretary, Budget

Bruce S. Wolff, Deputy Assistant Secretary for Legislation, Designate

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

NATIONAL INSTITUTES OF HEALTH

Statement by the Director

I am here to discuss with you today the 1980 budget request for the National Institutes of Health.

Although the figures in this budget are approximately identical to the 1979 appropriation, I come before the Subcommittee to assure you that the various programs of the NIH will be able to continue the level of excellence you have come to expect of us.

Maintenance of this level in a time of severe budgetary constraints represents a firm commitment by the Administration to the notion that the individual and societal costs of disease and disability can best be reduced through development of new approaches to prevention and treatment--approaches that depend in large measure on elucidation of the mechanisms underlying fundamental biological processes and an understanding of what happens when these fail or are altered to produce disease.

Maintenance of a level budget will impose difficult choices in the management of the biomedical research enterprise, and I am pleased to report that we are making significant progress in our ability to deal with some of the choices we face.

We now classify all of our programs as they relate to the four areas comprising the NIH mission to improve the Nation's health. The first of these, termed the science base, accounts for 74 percent of

the overall 1980 NIH budget request. It is science after all—the acquisition of new knowledge--which provides us with the tools we require to develop the ultimate means to reduce health care costs through preventing and treating more efficiently disease and disability. Thus, the manner in which research results are put to use comprises our second category--application—which depends intimately and entirely upon the success of our research programs. The third category, which we term "transfer", is an essential function of NIH and simply means that, once we know something important, we must make sure that the rest of the world knows about it too, and as soon as possible. It is especially important that physicians and health professionals put into use the most advanced methods available without delay. The fourth category, training, is, of course, the means by which the NIH and the Nation can continue the high quality of research for which we are acclaimed.

I cannot over-emphasize how absolutely vital the continued support of NIH's science base must be. I would like to take just a few moments to illustrate some of the recent advances in biomedical research and how this new knowledge is continually offering us potentially beneficial applications. The history of science is replete with examples to support this view. Recent advances in the use of recombinant DNA techniques have yielded new insights into the structure and regulation of genes, offering the possibility of commercial production of scarce biological products, such as insulin and growth hormone. It has moved us several steps closer to knowing the underlying causes of cancer, and to realizing the effective treatment of some genetic diseases. "Basic"

research in receptor sites--characterizing the interaction of hormones and cell surfaces--holds promise for the treatment of endocrine diseases such as diabetes. And investigation of the differences between normal and cancerous cells, while directed at the most fundamental biological processes, has significant implications for the diagnosis and prevention of cancer.

Certain elements of the science base deserve special mention. As Congress has recognized in recent hearings and reports, the primary mechanism for knowledge development is the investigator-initiated research project. Approximately 43 percent of the 1980 funds requested will support extramural research projects, allowing us to fund about 20 percent of approved competing grant applications. Supplementing the individual and program research projects are the research centers, where multidisciplinary interaction and support enable us to focus research in specific areas, such as heart disease and cancer. I share this Committee's concern that NIH grant programs be supported by a strong peer review system, and I am pleased to report the addition of four badly needed new study sections whose charters have recently been signed by Secretary Califano.

Our own intramural research program, conducted mainly in laboratories and clinics on and near the NIH campus, engages the efforts of approximately 60 percent of our staff. Evaluations of this program have repeatedly shown that intramural scientists' contribution to the science base far exceeds that which one would expect, based on their numbers. A recent evaluation shows the output of "most cited papers" between

1961-1975 by NIH intramural scientists to have exceeded by far any university in the world. There is no question that this select group of highly competent individuals, which includes four Nobel laureates, represent a major national asset, providing leadership to the biomedical research community and serving as a valuable resource to the extramural program staff.

The Clinical Center on the NIH campus provides unique opportunities for bringing the intramural science base to the point of application, a capacity that will be greatly enhanced by completion of the Ambulatory Care Research Facility. The final funding for the ACRF was provided last year, and construction is progressing smoothly; we look forward to its opening in 1982.

The application of research findings and development of interventions aimed at specific problems of health and disease represents the next step in the research continuum. Among the more exciting topics to be explored are development of systemic anti-viral agents and application of positron emission transverse tomography (PETT) for diagnosis of intracranial lesions. Also planned are several major clinical trials, including a joint effort between NHLBI and NIA to determine the effectiveness of lowering blood pressure in the elderly.

In recent years we have made significant progress in fostering the transfer of research findings to the health care delivery system. The Office of Medical Applications of Research, now officially established, serves as the focal point for NIH transfer activities, as well as a link to the broader mandate of the new National Center for Health Care

Technology. One of the key elements in this process is the development of consensus about treatment modalities. Over a dozen conferences have been held on a number of topics for this purpose and several more are planned. In keeping with our heightened interest in prevention, we have recently concluded a conference on antenatal diagnosis. The proceedings of these meetings are disseminated to both scientists and practicing physicians to further inform the general public.

The training of biomedical investigators remains one of the most critical activities supported by the NIH. All of our research training programs have now been consolidated under the National Research Service Awards program, and recent amendments to that law have done a great deal to make these awards more attractive to young scientists. The NIH has put forth a great deal of effort in the past year to develop a training policy truly responsive to the Nation's needs for the training of research personnel, as recommended by the National Academy of Sciences. The 1980 budget contains a modest increase for research training, which will be directed primarily toward training of epidemiologists and environmental toxicologists, who are needed to implement the new incentives in disease prevention. The budget request will provide for the training of approximately 10,900 investigators, an increase of some 375 over the current year's program.

Within the budget request, several areas of emphasis have been identified. Foremost among these is the Secretary's initiative in

prevention. Much of the NIH program is, at least indirectly, related to prevention, because the ultimate objective of most biomedical research--the understanding of life's most fundamental processes—will provide us with the means to prevent disease and disability. The redirection of funds within the budget will permit more rapid exploitation of certain high-priority areas, particularly those which lend themselves to enhanced cooperation and coordination among the Institutes of NIH and between NIH and other agencies. For example, toxicology research will be expanded to include additional studies of the effects of environmental agents and pollutants on human health, and the training of additional environmental toxicologists. This expansion will take place within the newly established National Toxicology Program which will provide coordination, under the leadership of the Director of the National Institute of Environmental Health Sciences, of all the Department's programs in toxicology.

International health is another area to be highlighted, focusing primarily on tropical disease and infectious diseases of international concern. The National Institute of Allergy and Infectious Diseases will serve as a focal point for international collaboration between the United States and foreign investigators.

As mandated by the Congress last year, diabetes continues to be an area of strong emphasis in many of the NIH Institutes. Recently, I directed the National Institute of Arthritis, Metabolism, and Digestive Diseases to assume the leadership role in coordination of all NIH diabetes research activities. It is our hope that this will serve as a model for

management of the many crucial research efforts that cut across Institute lines. The NIH commitment to diabetes research will continue to be strengthened in 1980, and the budget request includes an estimated $125 million for diabetes research.

Nutrition is another area of trans-NIH interest which offers great promise for the management and possible prevention of many disease states. Its importance is highlighted by the many Congressional mandates directed at NIH and other agencies. Research in nutrition continues to shed light on ways in which the body utilizes nutrients and how certain dietary substances may be related to diseases with a high incidence in the American population. We are expanding our support of clinical nutrition research units to include core grants for shared facilities combining research, training, and service. We expect to have several such units underway by the end of the year.

Mr. Chairman, I and the other Directors will be pleased to try to answer any questions that you or your colleagues may have.

APPENDIX D

DEPARTMENT OF HEALTH AND HUMAN SERVICES

PUBLIC HEALTH SERVICE

NATIONAL INSTITUTES OF HEALTH

Statement by the Director

February 5, 1980

Mr. Chairman and Members of the Committee:

I welcome the opportunity today - my fifth as Director of the National Institutes of Health - to appear before the distinguished Chairman and members of this Committee to testify on behalf of the President's budget request for the National Institutes of Health. Both the preparation for these hearings, and the discussions generated by the Committee continue to be most helpful to me in carrying out my responsibilities during the rest of the year.

The importance of these hearings derives from two basic facts with which you are familiar: the NIH is the Nation's largest biomedical research institution, and it is also by far the largest single source of funds for biomedical research conducted in the universities, medical schools, and research institutions of this Nation. Together these activities will determine much of the quality of health care for tomorrow, and sustain the quality of health professional education today. Thus the total resources of the NIH translate quite directly into the Nation's capability and achievement in the health sciences. Although our country's leadership here is being challenged, we are still extremely powerful and influential in this area of human service.

Last year I described our efforts to set biomedical research priorities in line with budget constraints. This year a formal planning process was extended to the Department's entire health research budget to seek greater efficiency and cohesiveness in the conduct of health research.

One focus of the planning process implemented by this year's budget is the Administration's commitment to sustain one of the major activities aimed at enhancing the science base. An important part of such research is provided by investigator-initiated research project grants awarded by the National Institutes of Health. These have been selected for emphasis to signal the recognition of the Nation's intent to maintain fundamental research as an indispensable long-term societal investment. Proof of this intent is absolutely necessary to assure that young Americans will continue to make the sacrifices necessary to invest their careers in the health sciences.

The number of competing projects funded in a given year has the virtue of allowing us to predict the numbers of scientists who can count on this type of support. The ability of the NIH to fund about 5,000 competitive projects or about one-third of approved grant applications in 1981 testifies to the Administration's determination to protect the national commitment for this type of research from the erosion of inflation.

It would be inappropriate and inaccurate, however, to create the impression that support of investigator-initiated research project grants is the only critical demand that must be met in biomedical science. The government's intramural research programs offer indispensable, and sometimes unique forces in the quest for scientific

information relative to agency missions. Our own NIH intramural program serves as a benchmark of excellence for our Nation's biomedical research community.

Approximately 70 percent of the NIH staff are associated with research conducted in the laboratories and clinics of the National Institutes of Health. Recent evaluations of the intramural research program give clear indication that it provides a milieu for research productivity that is second to no other institutional form. There is no question that the assets of the intramural program at NIH: the scientists, their supporting co-workers, and the facilities at its several campuses, are invaluable and irreplaceable national resources.

As the Committee is well aware, the NIH Clinical Center is a unique institution. It is the Nation's, and the world's, largest hospital dedicated totally to research on the diseases of mankind. The Ambulatory Care Research Facility (ACRF) which will be integrated fully with the Clinical Center, and whose construction has been supported and funded by this Committee, is nearing completion.

The ACRF construction is accompanied by some essential modernization of the Clinical Center. I am pleased to report to you that for this modernization program the Buildings and Facilities appropriation request contains $7 million in 1981 and a proposed $7.23 million transfer in 1980 from the Institutes with programs in the Clinical Center . This is a part of a continuing effort begun in 1979 to integrate the Clinical Center with the new ACRF and to correct functional obsolescence and physical deterioration in the parent hospital facility. The 1981 budget also contains $1.5 million for the initiation of a multiyear project to modernize other NIH laboratory

buildings which have been operational since the 1940's.

Various components of the new NIEHS facility are being completed and turned over to the Government. Our budget request for NIEHS contains $5 million and 55 positions for support staff and equipment needed to operate its new facility in North Carolina.

Other biomedical research needs are reflected in this budget as well. Last year, with your support, NIH, for the first time in six years, increased its stipend levels for the National Research Service Award program. This budget provides a further modest but essential increase in these stipend levels to partially compensate for the effects of inflation.

We are also requesting $1 million for an effort to attract promising minority high school students to careers in biomedical research. This program of short-term research experiences is a continuation of a program started in FY 1980 as part of the President's initiative to improve minority access to research careers.

Exciting advances are occurring across the full spectrum from fundamental research through clinical applications to the impact on health, care and prevention. Only three examples illustrate some of the far-reaching consequences:

Promise that greater control of the immune system may enable us to reduce or eliminate tissue destruction in such chronic diseases as arthritis.

Expectation that recombinant DNA technology will permit efficient manufacture of potent biological substances, such as insulin and interferon, and improve current vaccines.

Transfer to general medical practice the results of the recently

completed clinical hypertension trial conducted by the National Heart, Blood, and Lung Institute, revealing that treatment of mild hypertensives reduces rates of death and disability.

This year sees the fulfillment of the dream of former Senator Lister Hill that the National Library of Medicine enhance its information dissemination activities through the use of advanced technology. The completion of the Lister Hill Biomedical Research Communications Center will permit the National Library of Medicine to play this enhanced role.

The National Toxicology Program (NTP) has completed its first year and demonstrated it can join the research and regulatory agencies in common cause to determine toxicity of chemicals in the environment. NIH will increase its support for this program by $20 million, largely through a redirection of funds, in the National Cancer Institute and by $3 million in the National Institute of Environmental Health Sciences. With the increase, the NTP will begin 100 new bioassays for carcinogenicity, bringing the total at the end of the year to 320 bioassays in 1981 compared with 199 and 241, respectively, at the end of fiscal years 1979 and 1980.

The intramural programs of the NIEHS will be expanded by $3 million in such areas as pathology, behavioral toxicology, and development of test procedures and risk assessment which are especially important to the National Toxicology Program.

Adjustments cannot be made in one portion of the research budget without correction for the balance of the rest. The time scale for appropriate adjustment is often longer than a single year. Although the primary focus in Fiscal Year 1981 is on extramural research

projects, activities such as clinical trials, research centers, demonstration programs and interdepartmental initiatives will continue to be strong elements of the NIH program.

NIH recognizes that there are increasing pressures on the equipment and flexibility of the institutions in which much of the nation's research is carried out. This budget contains an increase of $5 million to improve instrumentation in extramural laboratories. We will be continuing our review of the research environment this year, in the company of scientists and administrators of their institutions. We hope to discuss the results of this review with Congress in the coming year.

I will close by saying that I am prepared to answer any questions you may have concerning the National Institutes of Health and our 1981 budget request.

APPENDIX E

TENTATIVE AGENDA
THIRTY-NINTH MEETING OF THE
ADVISORY COMMITTEE TO THE DIRECTOR, NIH
December 4-5, 1979
Building 31, Conference Room 10
National Institutes of Health

Tuesday, December 4

Morning Session

9:00	Overview on the Report: Health Research Planning in HEW--Analysis of Current Effort and Proposed Research Initiatives.	Dr. Fredrickson
9:30	"Stabilization" of the Science Base: Investigator-Initiated Research Project and Program Project Awards.	Dr. Raub
9:45	Committee Discussion	
10:15	Coffee Break	
10:30	Impact of Stabilization Initiative on Other Science Base Elements: NIH Intramural Program. .	Dr. Goldberger
10:45	Committee Discussion	
11:15	Impact of Stabilization Initiative on Other Science Base Elements: Research Resources and Centers	Dr. Raub Dr. Schneyer
11:45	Committee Discussion	
12:30	Lunch	

Afternoon Session

1:45	Impact of Stabilization Initiative: Applications and Technology Transfer	Dr. Gordon
2:00	Committee Discussion	
2:30	Long-Range Planning for Health Research: Institute of Medicine Perspectives.	Dr. Hamburg
2:45	Committee Discussion	

3:15	Research Planning and Budgeting: Perspectives from the Office of Science and Technology Policy . . .	Dr. Omenn
3:30	Committee Discussion	
4:00	Coffee Break	
4:15	DAC Perspectives on Health Research Planning. . .	Dr. Bennett Mr. Bennis Mr. Schmidt
4:45	Committee Discussion	
5:15	Adjourn	

Wednesday, December 5

Morning Session

9:00	Overview on Public Participation in Planning and Priority Setting	Dr. Fredrickson
9:15	Public Participation: National Science Foundation Perspectives	Dr. Atkinson
9:30	Committee Discussion	
10:00	Coffee Break	
10:15	Panel Discussion: Public Participation in NIH Advisory Groups:	
	Study Sections.	Dr. Butcher
	Advisory Councils	Mr. Takamura
	Recombinant DNA Advisory Committee	Mr. Thornton
10:45	Committee Discussion	Dr. Wexler
11:30	Concluding Comments.	Dr. Fredrickson
11:45	Adjourn	

ADVISORY COMMITTEE TO THE DIRECTOR, NIH

Minutes of Thirty-Ninth Meeting,
December 4-5, 1979

The thirty-ninth meeting of the Advisory Committee to the Director (DAC) was held on December 4-5, 1979, at the National Institutes of Health, Bethesda, Md. Dr. Donald S. Fredrickson chaired. (See Attachment 1 for lists of members and consultants.)

The focus of the first day's discussion was the recently completed HEW Health Research Planning document and the issues related to one of the main initiatives--Stabilization of the Science Base. The second day was devoted to a review of public participation in research planning and priority-setting.

Dr. Fredrickson noted that the last two meetings of the Committee had been devoted to reviewing the proposed principles for HEW support of health research and the larger process for development of a research strategy within the Department. At the last meeting (May 29-30, 1979), application of the "SATT" model (Science Base, Applications, Technology Transfer, and Training) to NIH budgets was considered. Specifically, the Committee had examined "stabilization" of a major element of the Science Base--investigator-initiated research grants (traditional research projects and research program projects). To highlight that discussion, various projections were shown for stabilizing the number or dollar-level of such grants over the next 5 years.

Since the May meeting, final HEW Health Research Principles have been approved by former Secretary Califano and released to the public (August 2). A draft HEW Health Research Planning document, based on these principles, was recently submitted to Secretary Harris for her consideration. It is believed that she will approve the document shortly for public release and comment. The document consists of two parts: an analysis of all HEW health research activities for FY 1980, and a proposed set of HEW multiagency health research initiatives for FY 1980-1984.

Dr. Fredrickson then noted that the proposed initiative relating to stabilization of the science base is being considered as part of the NIH health research planning process, which includes annual planning reviews with each of the Institutes. In this fall's planning reviews, each Institute's entire research portfolio is being examined relative to the stabilization initiative. Such reviews provide an opportunity for the NIH Director and his staff to discuss with the Institute Directors and their senior staffs the prospects and possibilities before the Institutes. Dr. Fredrickson remarked that this was the first time that National Advisory Council members, as well as members of the DAC and consultants, have been invited to participate in the reviews. Previously the reviews were open only to NIH Institute Directors and key staff.

To prepare the DAC for greater involvement in health research planning at NIH, today's meeting includes a review of the issue of stabilizing investigator-initiated research grants and the implications for the rest of the NIH programs. Specifically, the review will focus on the impact of stabilization on other Science Base components--research centers and resources and the intramural program--and on the other SATT categories--Applications, Technology Transfer, and Training.

Dr. Fredrickson also noted that at the last Committee meeting, Senate bill 988, sponsored by Senator Kennedy, was reviewed. This bill has not yet been reported from the Senate Committee, and whether there will be Congressional action on it is unclear. However, it is noteworthy that the bill proposes a Presidential Commission to oversee health research planning for the Department and the Federal Government. It is possible that the DAC might be considered as a mechanism for meeting long-term health research planning needs raised in the bill and in the Institute of Medicine's report on the principles.

"Stabilization" of the Science Base: Research Project Grants

Dr. William Raub, Associate Director for Extramural Research and Training, reviewed the SATT model and the elements that constitute the Science Base. (See minutes of the May 29-30 meeting for an explanation of the SATT model.) He then reviewed the principal causes of real or apparent year-to-year fluctuations in the opportunity to make research project grants and the steps NIH could take to make this aspect of its programs more nearly stable and predictable. He demonstrated these concepts under a set of theoretical assumptions or conditions and indicated implications for the rest of the NIH program.

Dr. Raub's first slide (Chart 1) showed the effect of holding research project grants (R01s, P01s, R22s, and R23s) to the same dollar level in FY 1980 and FY 1981. (See charts in Attachment 2.) If all prior commitments for research project grants running more than 1 year were honored (in keeping with a longstanding NIH practice), the number of new and competing renewal grants in FY 1981 would be limited to 3,350. Again, if the level of competing grants were stabilized at 4,900 through FY 1984, the total number of research project grants would increase slightly from 16,325 in FY 1980 to 16,475 in FY 1981 and then decline, as shown in Chart 2. Dr. Raub noted that the average life of these grants is 3.2 years.

He then reviewed briefly a projection (Chart 3) under conditions that assumed (1) stabilization of competing awards at the 4,900 level over the next 5 years, (2) an annual inflation rate of 8 percent, and (3) a comparable annual growth in the total NIH budget. A companion slide (Chart 4) illustrated the same model in terms of actual purchasing power.

Another model (Chart 5) presupposed no increase in the total NIH appropriation over 5 years and yet stabilization of competing grants at 4,900. Under this paradigm the "all other" category would be reduced from a $1,306 million in FY 1980 to $762 million in FY 1984. Inflation (at 8 percent per annum) would reduce the latter figure to $559 million in terms of purchasing power (Chart 6).

Dr. Fredrickson stated that subsequent discussion by NIH staff and DAC members at this meeting would focus on stabilization under conditions of no growth in total dollars.

The question was raised whether these figures took into account indirect costs, as indeed they did. Dr. Temin stated that indirect costs have been rising. Dr. Raub agreed that this was true over the past decade or so, but noted that over the past 2 years they appear to have stabilized at about 27 percent of total costs. There was a discussion about the concept of indirect costs and institutional ability to support research. Dr. Sullivan emphasized the need for adequate institutional support to provide a healthy research environment.

Dr. Bondurant felt it was important to specify what it was we wished to stabilize. Was it the budget, the number of projects, or the number of principal investigators? Moreover, does stabilization imply a floor or a ceiling? Dr. Fredrickson responded by stating that stabilization speaks to a need for predictability of Federal support for science. He noted that as part of vigorous Federal support, there is a need to assure continuing opportunity for competent principal investigators. He pointed out that this past year Congress for the first time has begun to look at support for a certain number of grants as an indicator of appropriate support levels, rather than concern itself mainly with funding levels for particular disease problems. Dr. Fredrickson added in passing that most recent data show one grant supporting 2.7 researchers, so that 1,000 grants support approximately 2,700 researchers. He emphasized that stability speaks to a floor--a minimum standard for support--and certainly not to a ceiling. Mr. Schmidt commented that the issue under discussion represented a "dilemma" rather than a specific proposed policy.

Discussion then turned to the probable effect on institutions of underfunding research grants to spread award money further during a prolonged period of budget constraints. How long can an institution go on encouraging research by its staff if the award money doesn't cover actual costs of the research and its supporting environment?

Dr. Greco inquired how innovative or nontraditional ideas would survive in the system under such austerity. Dr. Fredrickson pointed out that half of all applicants for new grants are young investigators--the group from which innovative ideas are most likely to come. Dr. Thier and Ms. Wexler asked where compromises could be made. How much would other NIH programs be reduced, and which programs would be affected by the stabilization initiative? Dr. Fredrickson noted that that would be the subject of the next series of discussions. He emphasized, however, that if the NIH programs were faced with a flat budget and had to take proportional cuts, then the number of research grants would face considerable curtailment.

Dr. Fredrickson then asked Dr. Robert Goldberger, the new NIH Deputy Director for Science, to discuss the impact on the intramural program of meeting the costs of stabilizing the number of grants supported in the extramural area.

Impact of Stabilization Initiative on Other Science Base Elements: NIH Intramural Program

Dr. Goldberger reviewed the history of the intramural program, noting its strengths and many contributions to scientific knowledge. However, austerity is at hand, he stated, and this will profoundly affect the program and its future. He traced the pattern of intramural funding for the past year, for this year, and for the immediate future, adopting the theoretical assumptions already outlined by Dr. Raub. He noted that if the intramural budget were allowed to grow at only 7 percent per annum, the funds actually available for intramural research would diminish at an alarming rate. Even with the optimistic assumption that inflation would run no more than 10 percent a year, this would mean annual program shrinkage of 3 percent. But the high percentage of the budget committed to salaries and other mandatory overhead expenses increases the squeeze on funds for direct research costs. Under these circumstances, he proposed that major budgetary restructuring would be required to assure that the excellence of the intramural program is maintained.

Dr. Goldberger cautioned that it would be terribly destructive to the intramural program if an attempt were made to reduce mandatory expenses by instituting a reduction in force (RIF). This procedure, which is the only mechanism for reducing the work force quickly and significantly in the Federal system, discharges employees with least seniority, without regard to their relative productivity or creativity. In fact, some of the most creative younger scientists would be among the first to go. This is a procedure to be avoided, said Dr. Goldberger. Instead, every imaginative approach to reducing mandatory costs must be explored, including more sharing of equipment and supplies, waiting turns, doing without, even allowing the work force to diminish through attrition, though the intramural staff has already dropped significantly. Dr. Goldberger pointed out that the high quality of its scientific research protects the intramural program somewhat from the vicissitudes of the Federal budget system, but that it would be foolhardy to ignore the dire implications of the problems he had outlined.

Dr. Thier asked whether there was any possibility of assisting the intramural program with extramural funds. Dr. Goldberger noted that the intramural program must be balanced with the extramural. Its excellence must be maintained, he stated, but not at the expense of the grants programs.

Dr. Temin returned to the possibility of reducing personnel through attrition. It was mentioned that attrition has taken its toll in the intramural program over the past 5 years. Dr. Fredrickson, promising a further opportunity for discussion on the balancing of needs, emphasized that Dr. Goldberger had the critical task of protecting the scientific excellence of the intramural program in a very difficult period.

He then called on Dr. Solomon Schneyer, Director of the Division of Program Analysis, Office of Program Planning and Evaluation, to review possible impacts of the stabilization initiative on certain parts of the extramural program.

Impact of Stabilization Initiative on Other Science Base Elements: Research Resources and Centers

Dr. Schneyer noted that centers supported by NIH basically fall under two general categories--research and resource centers. Under each are certain subsets.

Research and Resource Center Awards

NIH-supported research centers are of four types--exploratory, core, specialized, and comprehensive. The main types of resource centers supported include animal resources, biotechnology resources, and general clinical research centers.

Dr. Schneyer reported that in FY 1979 NIH supported 411 research centers for a total of $245 million. There were 249 resource centers, funded for a total of $92 million. Dr. Schneyer then pointed out that there is no overall NIH program for centers--that, rather, the individual Institutes make use of a number of different center mechanisms, as outlined above. The data for FY 1977 show that 4,000 professional positions were supported by NIH research center awards, versus 31,000 under regular research grants.

Dr. Schneyer concluded by citing an NIH study conducted under a committee he had chaired which showed that centers generally have a strong clinical component and a multidisciplinary emphasis. The committee visited two institutions and concluded that the negative impact on the institutions that would result from the elimination of center grants would be severe, but is related more to the relatively large amounts of money involved than to the funding mechanism itself.

Committee Discussion on the Stability Issue with Respect to Centers

Several members stated that institutions depend on the support of centers for clinical research, teaching, and training. Dr. Schneyer was asked whether the centers were supporting increasing numbers of physicians, possibly accounting for a decline in physicians on research project grants. He responded that although centers accounted for a much larger proportion of "professional doctorates" than regular grants did, his data didn't give a direct answer to the question. Dr. Thier pointed out that at Yale only 15 percent of the decline could be accounted for by M.D.s on center grants.

Mr. Schmidt, speaking from experience in the cancer program, noted the frequent concerns that center grants were not as thoroughly reviewed as research project grants and that large portions of the cancer funds were going for comprehensive centers. He pointed out that "comprehensive centers," a Cancer Institute designation, does not imply funding for comprehensive services. He noted--and Dr. Schneyer's slides showed--that the Cancer Institute's funding is for core grants and that the center investigators must compete for research grants like any others.

Dr. Temin noted the rigor of the NCI review for center grants and asked whether the other Institutes had similar procedures. Dr. Fredrickson called on

several Institute representatives in the audience who described various processes for review, all similar to NCI's but with some differences.

Mr. Schmidt commented that the question is not whether centers are desirable or useful, but whether one wishes to fund by the center mechanism as well as by other mechanisms. In his view the center is a valuable intrument as used by the Cancer Institute. If the excellence of scientific research is the objective, then the issue is not one of centers versus research projects or program projects, but rather that all mechanisms should be used where appropriate. The objective should be scientific excellence, with similar rigorous review for all types of support.

The Committee then discussed the purpose of center grants. Dr. Bondurant noted that traditionally the purpose has been to support new areas of research and increased productivity in the areas of applications and technology transfer and, further, to encourage multi- and interdisciplinary approaches to clinical research.

Dr. Hamburg observed that apparently there has been something of a national aversion to interchange between those in basic research on the one hand and those in applications/transfer on the other, and that centers serve to bring these communities and objectives together. Thus, centers should be a locus for stimulation of applications work from the science base and of science base work from applications. Dr. Hamburg asked whether there was evidence that centers are indeed performing these functions. Dr. Schneyer said that hard data are lacking, but program managers in the Institutes share the view that the center mechanism does advance multidisciplinary approaches.

Dr. Hansen emphasized that one should not consider centers as a unitary concept, noting Dr. Schneyer's observation of the many types of centers ranging from resources to cores for clusters of research projects. Dr. Bennett noted that the center mechanism has stimulated a great deal of interdisciplinary planning at institutions. In his experience, even if the grant is not awarded, it pays off in the institution by bringing the disciplines together. Dr. Fredrickson concluded the discussion by stating that, in his view, the primary function of the center is not to encourage multidisciplinary approaches, but to further the synthesis of research and applications, with a clinical dimension permitting outreach and transfer. He noted that any significant reduction of center programs would be risky for science, especially in terms of meeting health care needs.

Stability and Research Resources

Dr. Fredrickson then called on Dr. Raub to discuss research resources. Dr. Raub reviewed the major components of the resources program as an aspect of the science base. Approximately $20 to $22 million goes for animal resources, $59 million for general clinical research centers, $14 or $15 million for technology programs, $45 million for biomedical research support grants, and $14 million for the minority biomedical support program--a total of about $155 million. Dr. Temin commented that this money subsidizes ROIs and asked whether NIH has any figures on the extent of this. It was said that there are no data for that kind of breakdown.

Dr. Fredrickson added that another resource one must keep in mind is the National Library of Medicine, which accounts for approximately 1 percent of the NIH budget. He then called on Dr. Martin M. Cummings, the Director of NLM, to comment on austerity and its implications for the Library. Dr. Cummings stated that inflation runs twice as high in the library sector as in the biomedical research sector. He noted the fiscal constraints, but emphasized that personnel curtailment has backlogged several tasks of the Library, including the cataloging of all biomedical literature. Dr. Cummings then noted the enormous drain on resources for the regional biomedical library system and the serious cutbacks to be faced if there is no additional support.

Ms. Wexler raised the question of how many researchers are needed and can be supported. Have we reached the point where no more scientists can be sustained in the current pool? Dr. Bennis said that the question comes down to, How is one to make adjustments if everything is to be reduced? Mr. Schmidt pointed out that, in fact, with diminishing support over the past 4 years, most of the "fat" has been trimmed from the NIH budget, so that we are now talking about cutting out the core.

Dr. Fredrickson asked Dr. Riecken to report on the National Academy of Sciences' study of biomedical and behavioral research manpower needs. Dr. Riecken said that the Congressionally commissioned study has been under way for the past 3 years. The Committee, he said, has been asked to estimate the Nation's needs. These have been defined in terms of the market--namely, opportunity. Four reports have been issued.

They conclude that there is no significant unemployment in the biomedical field. There is, however, some underemployment in certain areas, such as toxicology, epidemiology, and biostatistics. There is overproduction of manpower in certain fields, with an accumulation of people in a postdoctoral holding pattern. At certain research-intensive universities, the postdoctoral scientists provide very good value for the dollars expended, but they are enormously burdened in terms of their career and salary. Dr. Riecken added that his remarks were limited to the academic sector. Finally, he said that the past 4 years have brought a downward adjustment in Ph.D. production in all fields, but with an attendant increase in graduate enrollment.

Dr. Fredrickson commented that if we want scientific research in this country, we must support training. Indeed, he said, approximately 5 percent of the NIH budget goes for training, and that, in his view, is an essential minimum for building future health sciences capacity in the United States.

Dr. Temin noted that one must consider in these discussions the impact of funding on different performers. These would include biomedical sciences nationally, individual institutions, individual departments, principal investigators, and other Ph.D.s and non-Ph.D.s. The key question in the long run is, How do we optimize progress? Mr. Schmidt and Dr. Thier pointed out that when one looks at the total national expenditure for health care, the portion for health research is quite small [about 3 percent]. And Dr. Fredrickson agreed that we are not, in that context, spending very much on biomedical research.

The Committee then concluded its discussion and adjourned for lunch.

Afternoon, December 4

Resuming the meeting, Dr. Fredrickson asked Dr. Raub to conclude the discussion on research resources by reviewing the NIH contract program. Dr. Raub reported that contracts count for approximately $500 million of the NIH budget. In SATT terms they are used principally in the Applications and Technology Transfer areas, much of this for the programs of the Cancer and Heart Institutes. He noted that there has been a progressive diminution in R&D contracts over the past 5 years because of greater opportunity for use of other instruments and because contracts at NIH require more personnel to oversee them than do the grants.

Dr. Fredrickson noted, however, that contracts are still crucial to such activities as the National Toxicology Program. The Cancer Institute has approximately $160 million in contracts, but that is declining every year. Dr. Sullivan asked why contract support is decreasing--especially in the cancer field. Mr. Schmidt explained that the contract program largely got under way at NCI in the 1960s when Congress made a special appropriation for virology research. To move as promptly as possible, the Institute used contract programs for this area, and as virology research grew, so did the support. It is becoming increasingly difficult, however, to use contracts in view of the administrative requirements. For basic research the grant mechanism is generally considered better.

Impact of the Stabilization Initiative: Applications and Transfer

Dr. Fredrickson felt that it would be worthwhile at this point to hear from Dr. Robert Gordon, Special Assistant to the Director, NIH, who would report on NIH activities included under the SATT categories considered as "Applications" and "Technology Transfer." Dr. Gordon stated that he would focus on NIH support for clinical trials, which account for approximately half of those activities. He chairs a Clinical Trials Committee that produces an annual inventory of all clinical trials supported by NIH. Because of the size and expense of clinical trials, sponsorship depends primarily on Government and industry.

Industry sponsorship of clinical trials is limited to those that evaluate a marketable product which, if successful, will bring profit to the sponsoring company. Most are carried out in support of applications to FDA for licenses to market. NIH may support trials related to a product that is in the public domain and not patentable, or that has too small a potential market to be of major commercial interest. It also sponsors trials of procedures, diets, or modifications in lifestyle that are not associated with a discrete product. The latter trials account for approximately one-fourth of the current portfolio.

Dr. Gordon then provided the following information concerning NIH commitments to clinical trials for FY 1976. There were 928 projects, for a total of approximately $121 million. He noted that the average trial takes 3 to 4 years, but some take up to 10. Thus, the concept of a commitment base is extremely important here, for the premature termination of a trial due to lack of funds would cause the loss not only of all the money invested but also of the patient's investment of discomfort and risk. Yet, if NIH tried

to stabilize research projects in a period of austere budgets, the effect on clinical trials would be amplified. Specifically, no new trials would be initiated.

Dr. Gordon concluded by mentioning the proposal that clinical trials be viewed as an evaluation of existing as well as prospective health practices. Hence, it might be appropriate for agencies such as the Health Care Financing Administration to set aside funds for this purpose. Conceivably, HCFA might join with NIH and the academic community in such an undertaking, with the former providing the funds and the latter providing the manpower.

Dr. Temin asked why HCFA and third-party payors should not cover those patient services within a clinical trial that are therapeutic and would have to be rendered anyway. Dr. Gordon replied that NIH already does this where possible, but that it is not easy to define the services that would have been provided in the absence of a trial. Dr. Thier asked whether NIH can provide data on its relative investments in clinical trials that seek new knowledge about disease, and in those that are primarily concerned with efficacy and efficiency in health care. Dr. Gordon replied that this distinction is not attempted in the ongoing inventory, and that meaningful data would be difficult to obtain, as the two types of objectives actually overlap and are intermingled in many trials. Dr. Temin asked how much it would cost, roughly, to support all the scientifically sound clinical trials proposed, and Dr. Gordon replied that the cost would exceed the total NIH budget if all that have been proposed were to be initiated concurrently.

Dr. Thier asked whether NIH had received many requests from HCFA to conduct clinical trials. Dr. Fredrickson replied that there have been only a few to date, but that the new National Center for Health Care Technology may occasion more. If there were to be requests, Dr. Fredrickson said, he would certainly recommend HCFA support for such studies. He also noted that the consensus development exercises under Dr. Seymour Perry at NIH are helping to meet HCFA's need for guidance in setting health care standards. He added that there will be a great need in this area and that several HEW agencies besides NIH will be involved. CDC, for example, clearly has a key role in terms of health promotion.

Dr. Fredrickson then concluded that the impact of stabilization had been a provocative and lively topic, but that other aspects of health planning must now be addressed. He called on Dr. David Hamburg, the President of the Institute of Medicine, for his perspective on health research planning and future needs.

Long-Range Planning for Health Research: IOM Perspectives

Dr. Hamburg noted his close association with the health research planning process over the past 2 years and his highly commendatory view of the work of the HEW Steering Committee and its chairman. He noted also that an HEW research planning document would soon be available, and that it would serve as an excellent followup to the health research principles document released last summer. He said that from his perspective the process over the past 2 years would be useful on a number of counts. It has much increased understanding and, with regard to the scope of health research throughout the Department, has helped the agencies to consider their missions and the gaps and overlap in research support.

He wanted us to know that the IOM, in reviewing the health research principles, had strongly supported positions on the issues under discussion at today's meeting. Namely, the IOM Committee endorsed long-term, predictable Federal support for health research, with a commitment to the training of future generations of scientists and to the renewal of the physical and human potential of institutions in the next decade. He pointed out other issues highlighted by the IOM Committee, such as a need to address the balance between established and new investigators and a need for higher levels of support to address the scientific opportunities open in a number of difficult health problem areas.

Dr. Hamburg then remarked that a key recommendation of the IOM Committee was for some permanent planning mechanism for long-range issues in health research. There is such a need not only for HEW but across the Government, including the Congress and the Office of Technology Assessment. Some issues requiring long-range planning include achieving appropriate balance for research among Science Base, Applications, and Technology Transfer, and between the Federal and private sectors, and among health agencies where priorities could be spread in the applied area. Such a planning mechanism, he said, assumed urgency because of the transitory nature of the high-level appointments within Government agencies. He noted, however, that neither he nor the IOM Committee has a preconception of the mechanism they proposed.

Dr. Hamburg concluded by stressing the importance of planning, especially as we enter a new phase of scarce resources nationally for all programs. With the energy crisis and the changing nature of our relationships with other nations, particularly in the Third World, we must recognize the limitations and attempt to anticipate them. Clearly, health research planning calls for new elements and new attention.

Dr. Fredrickson responded by acknowledging the invaluable assistance that Dr. Hamburg personally and the IOM Committee have been to him, to the Steering Committee, and to HEW Secretaries. He asked Dr. Hamburg whether he could suggest any long-range mechanism that might serve as a model. Dr. Hamburg said there were obvious models but they cannot be divorced from the clinical process. We need to strengthen the long-range view within the Department, and perhaps the model of the National Science Board would be one to consider. He noted that the National Academy of Sciences, as a body, provides some continuity for review and plans, and that several 5-year "plans" in the European countries were presented at IOM's meeting of the European Medical Research Council last spring. Perhaps one could learn from these countries, from the HEW Steering Committee, or from the Director's Advisory Committee what possible models might serve as useful forums.

Dr. Fredrickson thanked Dr. Hamburg and then called on several DAC members to present their views on health research planning.

DAC Perspective on Health Research Planning

Dr. Bennett opened by outlining his experience with planning boards in the fields of defense and energy. Most of the discussion, he said, was not on science but on management, and the boards attempted to advise program managers

on how to manage their budget but not on selecting priorities. Thus, one must distinguish between scientific questions and managerial questions. He emphasized that, in his view, planning must be under the immediate direction of the executives who have responsibility for management and budgeting, and cannot be an independent exercise. To think that planning can be separate from the responsibilities of the main executive officers is a vain hope. The plans, he believes, must come from managers assisted by staff and must tie into the budgetary process. This was his central lesson in dealing both with Government agencies and the academic sector.

Dr. Bennis commented that the meetings of the DAC he has attended have been enlightening forums for reviewing the NIH programs and issues. The focus of today's forum was on hard times. Clearly, in the face of austerity, planners must inform the broader community and constituencies about the nature of that austerity and suggest where adjustments should be made. He emphasized his clear agreement with Dr. Bennett that planning must be done by the managers and must be integral with the budeting process. He noted that today's discussion, in large part, was on allocation issues, but that a crucial question concerns the output of the process: What is critical, not only in allocation but in what the money is buying? That is an important element in all planning considerations.

Mr. Schmidt reemphasized the remarks on planning he had made at the last DAC meeting. (See minutes of the May meeting.) Here again, planning is essential in both the Government and the private sector, but it must be done under the chief executives. Further, plans should not serve as a crutch for decision-making by executive officers. Once the plan is formulated, it should not become the absolute guide for decision-making on day-to-day operations. He noted that the scientific community is skeptical about planning because many scientists believe it means directed research. The Cancer Plan has shown that this need not be the case. It has not led to centralized control through a Federal committee or agency. He added that the best tool in the corporate world for ensuring an effective plan and its implementation is to tie incentives into its realization.

Dr. Fredrickson agreed that planning must strongly involve the executive body. At NIH, research planning consists in his meeting with the Institute Directors, in detailed staff work for organizing the meetings, and in following up on the emerging issues. It takes an enormous commitment of both the staff's and his time, but he believes it is well worth it. The planning for NIH, he said, involves a number of functions, including anticipation of what will happen fiscally, decision-making on what must be done to inform the community, listening to the community's reaction, and coping with administrative and Congressional budgeting processes.

Ms. Wexler noted a difference between planning in corporations and in government. In corporations the executive officers and boards are relatively stable, whereas in government the managers frequently change.

Dr. Fredrickson concluded the discussion by stating that many important issues had been raised and that the DAC will continue to be involved in planning for NIH research. Further discussion will take place in January after the NIH research plan reviews, with DAC and consultant participation. Dr. Fredrickson then announced a coffee break. As he would have to be away from the Committee

for a short time, he appointed Dr. Bennett as acting chairman for the next discussion.

Research Planning and Budgeting: A Perspective from the OSTP

Dr. Gilbert Omenn, Associate Director for Human Resources and Social and Economic Services, Office of Science and Technology Policy, commented briefly on the HEW health research planning process. He noted that the process is open and highly responsible and has had the OSTP approval. He noted, however, that the focus has been more on process than on planning. He found that the National Conference on Health Research Principles was an attempt at openness and information exchange, but the five panels and scores of witnesses, as all agreed, had little opportunity to engage with one another, and opportunity for exchange was lacking, especially among the various disciplines represented. Now, with the health research principles approved, a critical question was, What impact, if any, would they have on planning within HEW? Dr. Omenn's impression was that they do not have much impact at present on major HEW research programs. He noted, for example, that the HEW planning document has initiatives on stabilization and the National Toxicology Program, but both have high Administration and Congressional priorities anyway. Although the plan speaks to many of the concerns raised by participants in the principles process, the crux is whether the principles can be used meaningfully to set research priorities.

Dr. Omenn then turned to the stabilization issue and commented that stabilization of support is the first priority of the Office of Science and Technology Policy. Although he was not present for the morning session, he recognized the impact that stabilization of research grants would have on other NIH programs. For FY 1979, about 15,800 research project grants were funded--a high water mark--because of the emphasis on basic research by the Administration and the Appropriations Committees. He recognized that this high water mark presents problems in sustaining the support for new grants. He believed, however, that the President and the Congress could support 5,000 new, competing NIH awards.

He then reviewed briefly, from his perspective, the effects on other NIH programs, as discussed earlier in the Committee meeting. Austerity would impact on centers and contracts. It would also impact on the intramural program, which may need a stronger identity to distinguish it from research activities in the academic and private sectors. He suggested that perhaps the intramural program should place more emphasis on doing what the universities cannot do, such as international epidemiology and overseas research work.

On the question of training, Dr. Omenn believes the Federal subsidy is necessary. The present support of higher stipends is critical here, and the Federal Government has lacked an overall view of training for biomedical research.

On the subject of clinical trials, he noted the difficulty of carrying them out and their need for continuing support.

The principles process helped, he feels, in identifying the needs of agencies other than NIH and exploring possible support mechanisms. He described an OSTP activity with the National Center for Health Care Technology on percutaneous transangeography (PCTA) and pointed out the need for collaborative

support among many agencies including the Health Care Financing Administration (HCFA).

Finally, Dr. Omenn noted that more attention has to be given to research resources. There has not been overwhelming support from the Hill in this area.

Dr. Omenn commented in conclusion that the planning exercise has been useful in identifying the research work of other agencies, in raising the question of balance among allocations, in providing public participation in the process, and in stimulating interest in research; but on the issue of priority-setting, there is still a question of how effective the principles or planning process will be. Clearly, however, a key priority is stabilization of 5,000 competing grants, with the public debate then focusing on allocation within other NIH programs.

Dr. Bennett, as acting chairman, requested Dr. Omenn's comments on the following three questions: (1) Does he believe that the present organization of NIH's categorical Institutes has been useful in drawing Congressional support to biomedical research? (2) Is there any point in searching for agencies other than NIH to do research in clinical applications and technology transfer, since the responsibility generally falls to NIH anyway as the last bastion for quality investigation? (3) Given this, could other agencies, such as HCFA, provide NIH with the money to do this work?

Dr. Omenn responded that the present structure of NIH largely reflects Congressional interest in the various categorical diseases and probably accounts for the fact that the NIH budget is three times that of NSF. But more coordination is needed among the Institutes, as in the area of training. Dr. Bennett asked whether he would favor reprogramming authority for the NIH Director. Dr. Omenn replied that at least for trans-NIH issues, the Director should have some discretion for their support.

He agreed that it would be useful for HCFA to provide funding for many clinical trials; that perhaps they might be able to fund some, even under their present legislative authority; but that their authority would have to be changed to permit a much higher level of funding in this area.

On the matter of public participation, Dr. Omenn believes Government processes are far more open now than ever before, and this has been good for science and the public. In his own experience on the Advisory Councils of Cancer and Heart, the lay members had been especially influential in the Council debates. He believes this is a healthy trend and will continue.

Dr. Temin asked whether the President's budget would speak to the other needs of the NIH programs if competing research grants were stabilized at the 5,000 level, especially in view of the morning's discussion about the drastic impact of constraints on total dollars. He was most concerned about what the President's budget would do to address this. Dr. Omenn said he could not respond specifically on the budget, but could say that the President would be attentive to assisting in the process of making necessary adjustments.

Dr. Bondurant questioned the wisdom of pursuing the stabilization question. Is this something that would be attractive on the Hill and as research strategy

for the '80s? Dr. Omenn noted that there has been Congressional support, but that budget austerity is a crucial issue for the Congress as well as for the Administration. The Appropriations Committees are scrutinizing the Federal budgets more closely than ever before and following the President's Budget recommendation more closely than in the past.

Dr. Bennett then turned the meeting over to Dr. Fredrickson, who had returned. Dr. Fredrickson thanked Dr. Omenn for his presentation and adjourned the meeting, announcing that it would resume at 9:00 a.m. for a discussion of public participation.

Morning, December 5

Dr. Fredrickson opened the second day of the meeting by commenting that the forthcoming discussion on public participation in planning and priority-setting is responsive to the key role of the public in support of the research enterprise. In other words, as a quid pro quo, the enterprise as part of its responsibilities must visibly attempt to meet society's needs for information that may be applied to health problems, must validate and otherwise assess potentially useful findings, and must take the additional steps in identifying and processing useful new knowledge to facilitate its translation into improved health care.

Dr. Fredrickson explored the question whether two levels of public involvement need to be considered. The first, which he characterized as a "macro" level, has always provided for some public scrutiny and interest, primarily in the context of Executive and Congressional processes of resource allocation and oversight. Since the 1950s NIH has been examined by at least 10 Federal and non-Federal commissions. The most notable of these have been the Wooldridge Committee, reporting in 1965, and ten years later, the President's Biomedical Research Panel. Congressional attention has taken the form of oversight hearings, the setting of time and dollar limits on research program authorizations, and special mandates. Dr. Fredrickson expressed the hope that this augmented dialogue with the Congress has been helpful.

On the "micro" level, NIH has a number of organizational structures that permit public participation in decision-making. For example, public representation is found at all levels of NIH program activity through the mechanism of Advisory Councils, which have a statutory requirement for lay representation. Also, the DAC with its trans-NIH responsibilities, has the potential for providing a functional interface between the public interest and both research and services. In light of this role, Dr. Fredrickson said the focus of the meeting today would be on the fifth (and broadest) of the Health Research Principles, which speaks to maintaining scientific excellence through the peer review system while providing for public participation in research policy- and priority-setting. He went on to note that considerable attention has been given in recent months to the peer review system, and that it was most important for the Committee to consider that system in the broader context of public participation. He then called upon Dr. Richard Atkinson, Director of the National Science Foundation, to discuss a recent study by NSF on public participation in science policy-setting.

Public Participation: An NSF Perspective

Dr. Atkinson opened by commenting that in 1976 Senator Kennedy inserted language in the NSF authorization act directing the agency to "facilitate the participation of members of the public in the formulation, development, and conduct of the National Science Foundation programs, policy, and priorities." On the basis of that mandate, the National Science Board (NSB) chose a series of regional forums as a means to obtain public participation. Six forums were held over a 2-year period in 6 different locations throughout the United States. In June 1979 the Board issued a report on the basis of these activities.

Dr. Atkinson said that the sessions at these meetings focused upon major regional science-related issues, such as the management of food and water resources and the development of energy sources and alternatives. Three policy issues faced by the NSB were also included: (1) how to increase participation of women, minorities, and the handicapped in scientific careers; (2) how to achieve balance between supply and demand for research personnel in scientific professions; and (3) possible funding of alternative performers of basic research beyond the traditional university clientele.

Dr. Atkinson reported that a survey of the forum participants disclosed the following: Approximately 21 percent conducted research on NSF projects; over half represented organizations that conducted some research; and slightly over a third of those organizations had received an NSF grant or contract. A third of the participants had received a Ph.D.

Participants, he said, were polled on what role they would assign to various groups in society for helping the NSB to establish priorities in the areas of basic and applied research and science education. On the basis of that poll, the scientists were given a role considerably above any other group in determining basic research priorities. In regard to applied research and science education, participants preferred a significant role for several non-scientist groups.

Dr. Atkinson noted that NSF is now digesting the report and considering what further steps should be taken. Some implementation of the findings has occurred through the modification of advisory committees to make sure of a broader representation, especially in the areas of applied research and science education. He also noted that there is now an advisory committee to the Director, NSF, with 24 members, 6 of whom are chosen to represent the public. He noted that the NSB is composed of scientific members who decide on the science programs and highly technical matters including allocations. The public members on the advisory committee speak to broader policy questions. Board members frequently attend meetings of the Advisory Committee, so there is good interchange between the two groups.

Dr. Atkinson stated that a major concern of NSF is not only public involvement but the adequacy of participation by the scientific community in the setting of priorities. He noted the difficulty in getting the scientific community and particular disciplines to agree on priorities--a process becoming more and more important in an era of austere budgets. Priority-setting, he said, can be achieved within fields, but it is much less effective across

fields and especially across Government agencies. Then he observed that basic research in the biomedical area has had far more Federal support than in the physical sciences under NSF, where there has been a drastic loss in buying power.

Dr. Fredrickson thanked Dr. Atkinson for his remarks and then invited Committee discussion. Dr. Bennett asked for more information on the advisory committee to the NSF director. Dr. Atkinson responded that the committee meets twice a year and selects various topics to pursue. The issues followed up have included, for example, support for young investigators, international science, the peer review process, and institutional cost-sharing for expensive instruments.

Mr. Takamura asked how public members are selected for the advisory committee. Are there any specific criteria? Dr. Atkinson said no, but that a number of names are reviewed from a variety of sources. Often critics of particular NSF policies are selected to serve on the committee.

Mr. Hutt noted that, at the FDA, policy and technical issues are frequently merged, with scientists and public participants combined. The public members are selected by public-interest organizations through nomination and voting. The process works well--indeed, has been so successful that the Congress in 1976 mandated that such mechanisms be employed on the technical committees reviewing medical devices. Could such groups be formed at NSF, or could laymen participate on the NSB and in peer review? Dr. Atkinson responded that the President selects the Board following scientific and lay nominations. Apart from that, it is a scientific group. It has made sense to maintain a distinction between the Board and the Advisory Committee to the Director.

Dr. Atkinson went on to say that, as the evaluation of former participants showed, priorities at a basic science level should be set by scientists, but in the applied research and technology transfer areas, as at the FDA, public participation with scientific expertise makes more sense. He also noted that NSF's system is different from NIH's in that the advisory and peer review panels are strictly advisory--that the program officers make the basic decisions on funding, with oversight by the NSF directorate. All actions, however, are reported back to the study sections and advisory committees.

In response to a question, Dr. Atkinson said that the NSB does not plan to repeat the forums.

Mr. Bennis asked how one organizes public participation and for what purpose? Dr. Atkinson responded that the most effective public oversight comes from the Congressional committees. Dr. Shaw inquired about NSF's science and technology program, and Dr. Atkinson described it as a small but important program that does include nonscientists. Mr. Hutt mentioned the difficulty in setting priorities for research training and manpower. Dr. Atkinson said it can be done, citing the field of high-energy physics as one that has been successful in priority-setting. Dr. Wu agreed that priority-setting had been successful in that field, where there was a scientific consensus. Dr. Atkinson said that, indeed, the work done there provides an excellent model for other disciplines.

Dr. Fredrickson concluded the discussion by noting that a distinction should be made between public participation that includes both lay and scientific members and participation that includes only nonscientists or nonexperts.

After a coffee break, Dr. Fredrickson said that the Committee would now hear from consultants who had been asked to give their views on public participation in NIH advisory groups.

Panel Discussion: Public Participation in NIH Advisory Groups

Study Sections. Dr. Reginald Butcher, who has served for several years on NIH study sections and most recently as chairman of the Metabolism Study Section, said that the purpose of the group is to determine the scientific merit of a proposal. It is not to make funding decisions or set national priorities. He noted the enormous work involved for those who serve on these panels. Many proposals have 70 to 300 pages, and some of them are assigned primary and secondary reviews, both requiring a written critique. In addition, the study sections meet approximately 4 to 5 days per year, usually in 12-hour sessions. There the critiques are thoroughly reviewed, and priority scores from 1 down to 5 are assigned. The Executive Secretaries prepare summaries and recommendations and pass them on to the relevant advisory councils.

Because of the highly technical nature of the work, Dr. Butcher believed it would not make sense for public members to serve on the committee and vote on the proposals. However, he thought it might be useful for public members to serve as nonvoting observers, suggesting that NIH consider this as a possible option.

Advisory Councils. Mr. Carl Takamura is a lay member of the Advisory Council of the National Institute on Aging. In his experience, the councils trust the study sections' recommendations and rarely act against them. They may do so, however, when they note a discrepancy between the priority score and the evaluative comments in the summary description. Occasionally the Councils recommend a higher priority for payment when a project has high program relevance, and sometimes the advisory councils ask study sections to look again at specific proposals because of relevance aspects. Mr. Takamura suggested that the nature and extent of lay participation on the councils should be spelled out more completely. He compared starting on an advisory council to entering a foreign country where the language and value system are strange and there is a set of "heroes and villains." The lay person ought to have some of this explained and be briefed prior to service.

Mr. Takamura's experience on a special program committee of the Aging Council has given him a far better grasp of the Institute's scientific programs. He proposed training for lay participants and suggested they be encouraged to sit in on one or two meetings of study sections and to participate in appropriate site visits. Indeed, he felt it might be useful for laymen to become acquainted with study sections as nonvoting observers before gradually becoming full members of advisory councils. He concluded, though, that it didn't make sense for public members to serve as voting members of study sections.

In summary, Mr. Takamura remarked that lay participation can be of great value for groups providing oversight and advice for the research enterprise. It encourages better public understanding of scientists, their institutions, and their values, and it also offers scientists a useful public perspective on their programs. Finally, he recommended that NIH consult with former public members of the advisory councils for advice on how public participation might be improved.

The Recombinant DNA Advisory Committee (RAC)

Mr. Ray Thornton, a former Congressman from Arkansas and past chairman of a House science committee, is a lay member of the RAC. This committee is unique at the NIH because it combines both technical and public policy review and includes both scientific and public participation. The RAC is responsible for making recommendations to the Director of NIH on all matters relating to recombinant DNA research and the NIH Guidelines.

Mr. Thornton noted that there are eight to nine laymen on the committee who are full voting members. The Committee scientists have taken the time to educate the public members patiently on science issues, and the process has worked extremely well. He characterized recombinant DNA as an especially interesting "case study" in which the scientific community itself raised the safety issue and, because of that concern, the Congress considered but did not pass legislation to regulate the research. With NIH leadership, the research has been able to proceed under appropriate safeguards. He concluded with the observation that science may be viewed as a driving force having two fronts--one, the technological consequences resulting in improved health and longer life; the other, the ideological and philosophical consequences of science--many of them unintended--that require a reappraisal of the nature of the world, ethics, morals, and government. It is with respect to issues in the latter area that public participation in oversight of science is most important.

Dr. Fredrickson thanked the three consultants for their excellent summaries and turned to Ms. Wexler to begin the Committee discussion. Ms. Wexler commented first on the importance of the public's having a meaningful role in science oversight activities and not merely being patronized. Thus, it should not be an occasion for the knowledgeable to present a veneer of public participation. There is a real need for creative tension and for honesty about the part that can be played by the public. Expectancies for the public may be raised that cannot be met. This has been one of the problems of the last decade as many professions and publics have sought to interact. She noted that it requires a great amount of time and effort to serve effectively as a public member of one of these groups.

Ms. Wexler agreed with Dr. Butcher that it would be worthwhile to have public observers at science panel meetings, but not as voting members. Public observers would be excellent in judging procedures but not scientific merit. She was pleased to hear Mr. Thornton describe his role on the RAC, where indeed it appears that public members have taken the time and been able to master the issues, contributing substantially to the governance of this research. And finally, she believed that public interest groups have an important role to play

on advisory committees, and that what is essential is to look at the concept of trusteeship--to gain trustees, be they scientists or laymen.

Dr. Bennett noted how far we have come to hear Dr. Butcher suggest that laymen be present at study sections. This idea would not have been entertained even 5 years ago. He has served on several committees where the contribution of lay members has been impressive. He specifically endorsed the concept of lay observers on study sections, and also the possibility of assembling lay alumini of advisory councils to get their views.

Dr. Shaw remarked that laymen do trust the judgments of scientists but that the scientists have been slower to recognize and trust the contribution of laymen. Dr. Bondurant said that it is not only laymen who face cultural shock--that even scientists on first coming into study sections must undergo a process of acculturation in dealing with the proposals and their evaluation. He suggested the possibility of forming a pool of laymen who have previously served on scientific committees, with a view to drawing upon "experienced lay advisor"; but he then noted that there may be a problem of co-option.

Mr. Hutt agreed with all that had been said about the participation of laymen on study sections and their not having a vote. He did have problems with the "training" of laymen to serve, noting that in his service on advisory committees, it was advantageous to have had to face the issues and force himself to understand and work through them. In short, it was better not to be trained or prepared. The critical need is to get people who will accept the commitment to do their homework. Dr. Greco observed that the average layman on these committees is not the average citizen--that these people are selected as having distinguished themselves at something.

Dr. Fredrickson concluded by commenting that today's excellent discussion should provide any committee at NIH with much material for consideration of this most important issue. He added that he would ask Jacqueline Wexler to follow up on some of the ideas expressed, perhaps in time for the next several meetings. He then thanked the participants and adjourned the meeting at 11:45 a.m.

Respectfully submitted,

Joseph G. Perpich, M.D., J.D.
Executive Secretary
Advisory Committee to the Director, NIH

National Institutes of Health
Bethesda, Maryland 20205
January 3, 1979

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December 4-5, 1979, Meeting of
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NATIONAL INSTITUTES OF HEALTH

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David Paige Smith Professor
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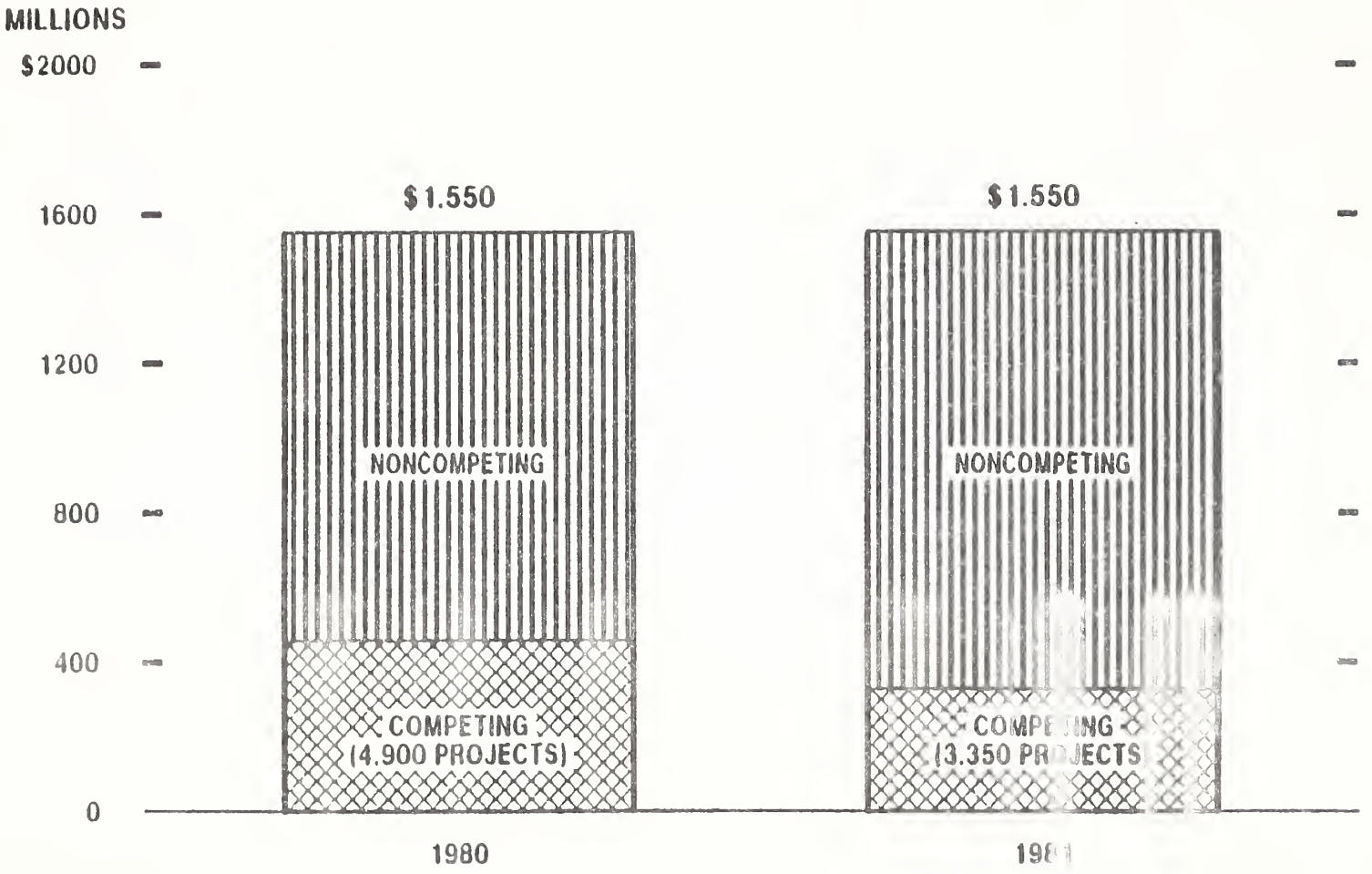
Department of Internal Medicine
Yale University Medical School

Mr. Ray Thornton
Joint Educational Consortium

Dr. Lewis Thomas
President
Memorial Sloan-Kettering Cancer Center

Chart 1

COMPETING RESEARCH PROJECTS FISCAL YEARS 1980 AND 1981 ASSUMING NO GROWTH



NOTE: 8% INFLATION ASSUMED FOR COMPETING RESEARCH PROJECTS AND COMMITMENTS MADE FY 1980 AND LATER.

Chart 2

NUMBER OF RESEARCH PROJECT COMMITMENTS DERIVED FROM FISCAL YEAR 1980 COMPETING AWARDS

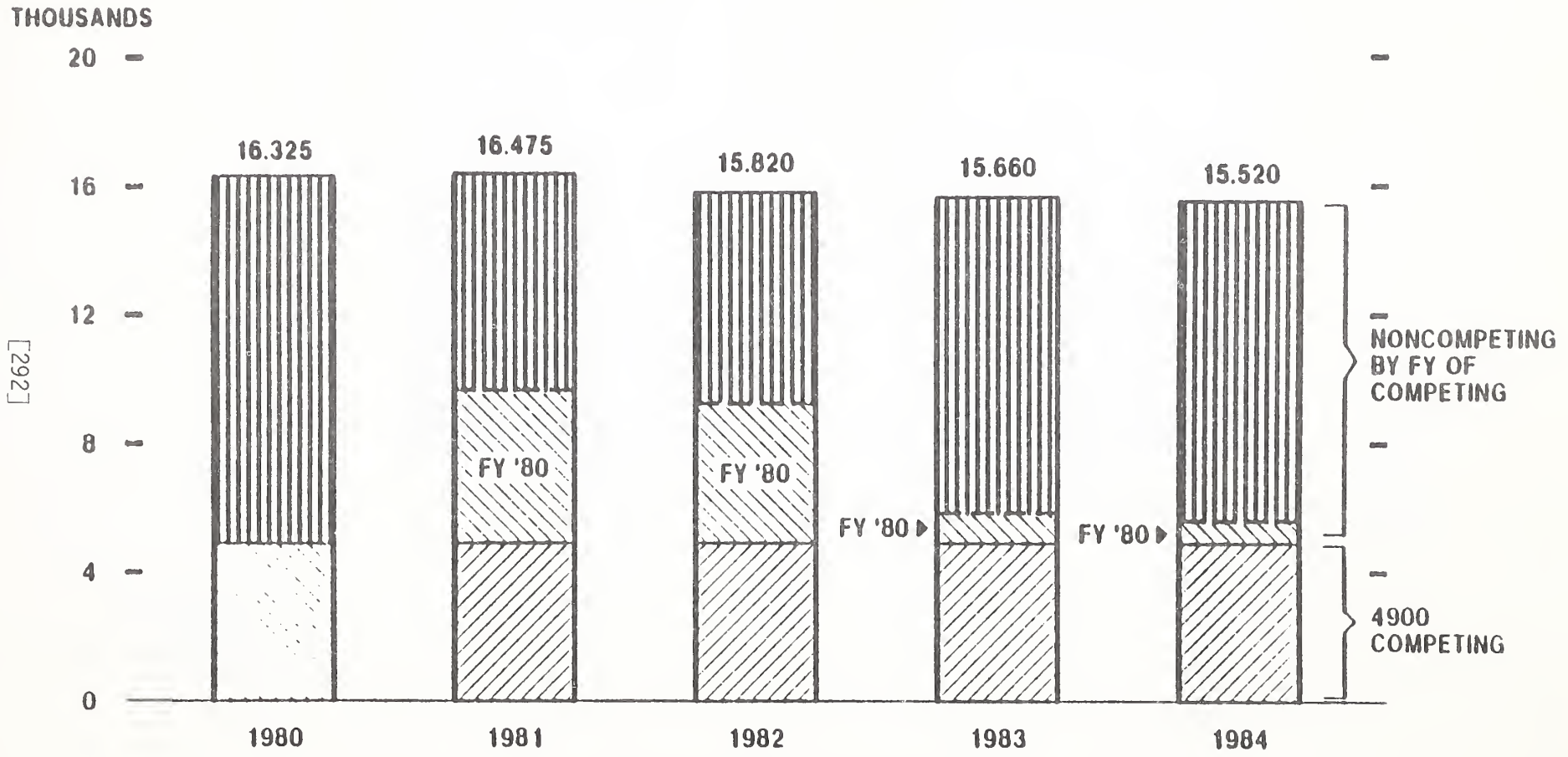
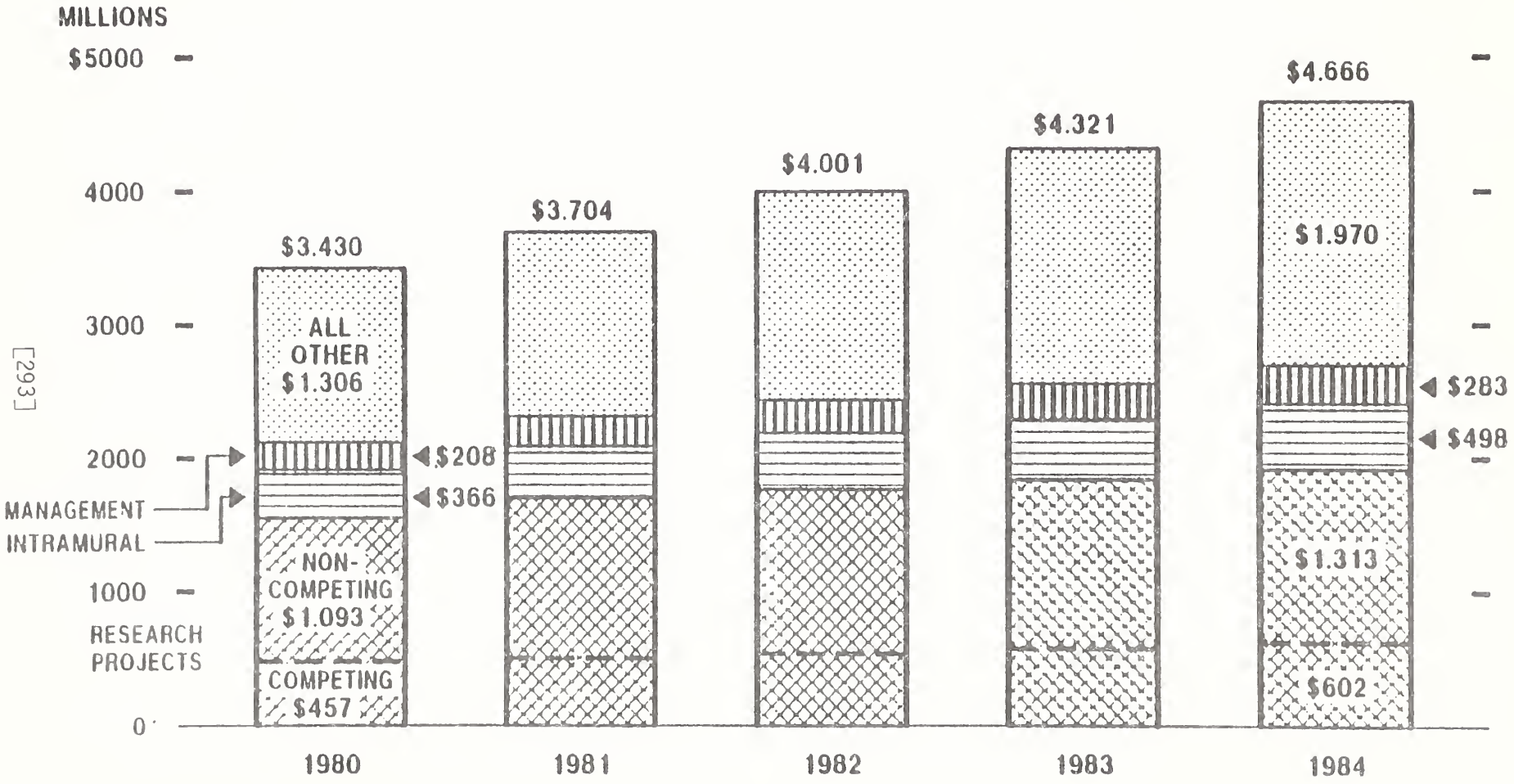


Chart 3

TOTAL NIH FUNDS. FISCAL YEARS 1980 - 1984
CONDITION 1

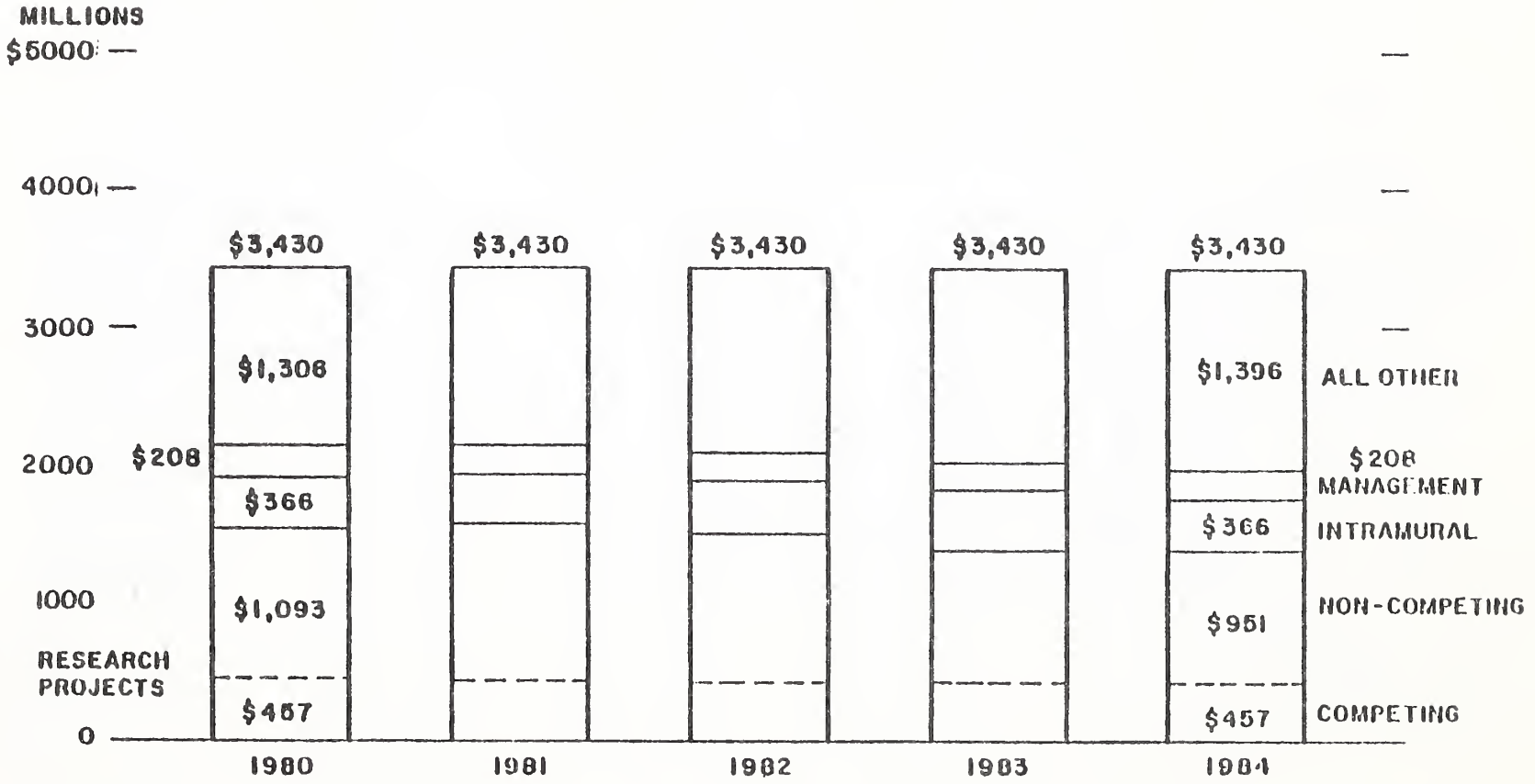


NOTE: 8% INFLATION ASSUMED FOR COMPETING RESEARCH PROJECTS AND COMMITMENTS MADE FY 1980 AND LATER.

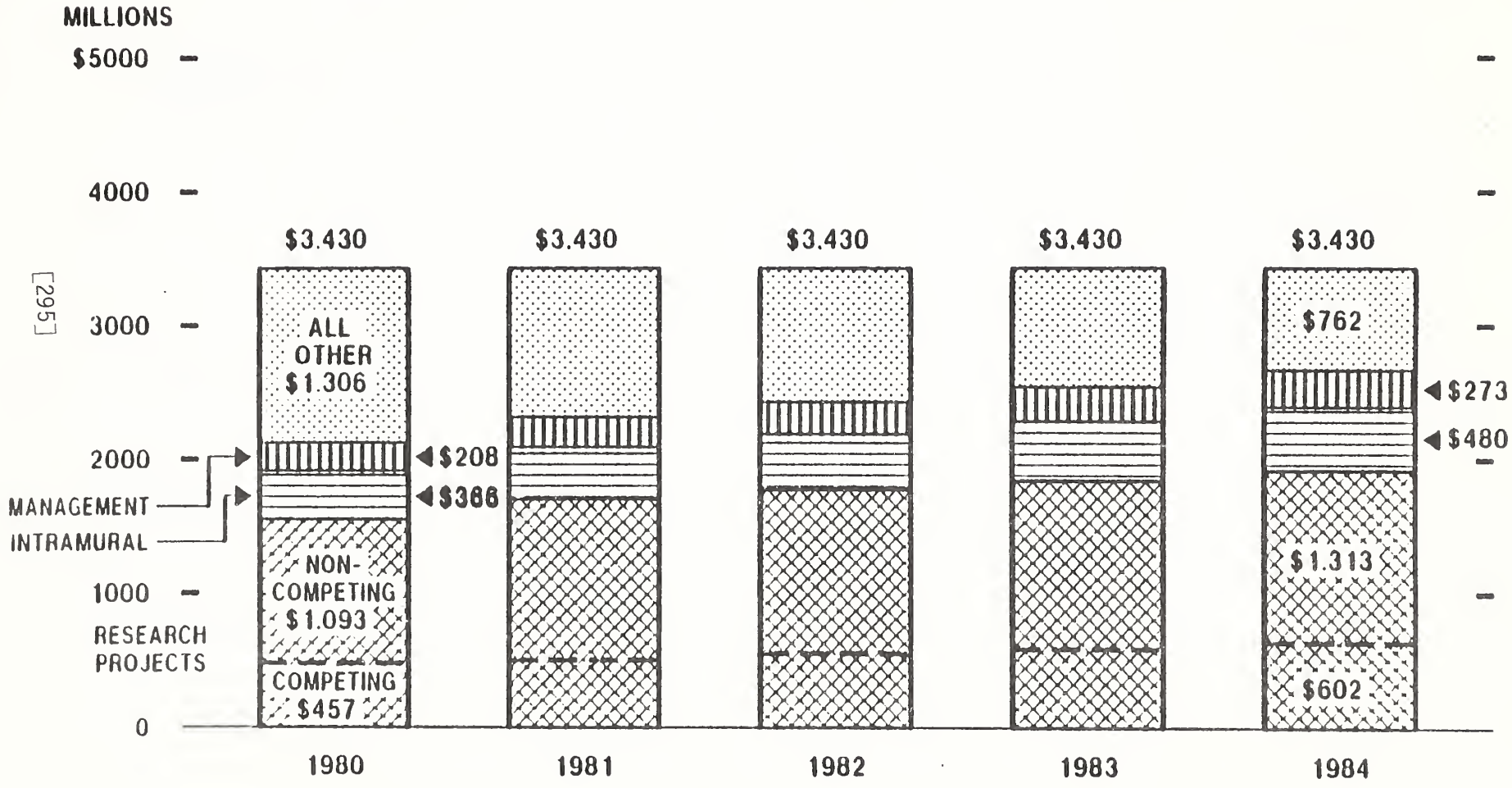
Chart 4

TOTAL NIH FUNDS, FISCAL YEARS 1980 - 1984

CONDITION I, IN CONSTANT FY 1980 DOLLARS



TOTAL NIH FUNDS. FISCAL YEARS 1980 - 1984
CONDITION 2

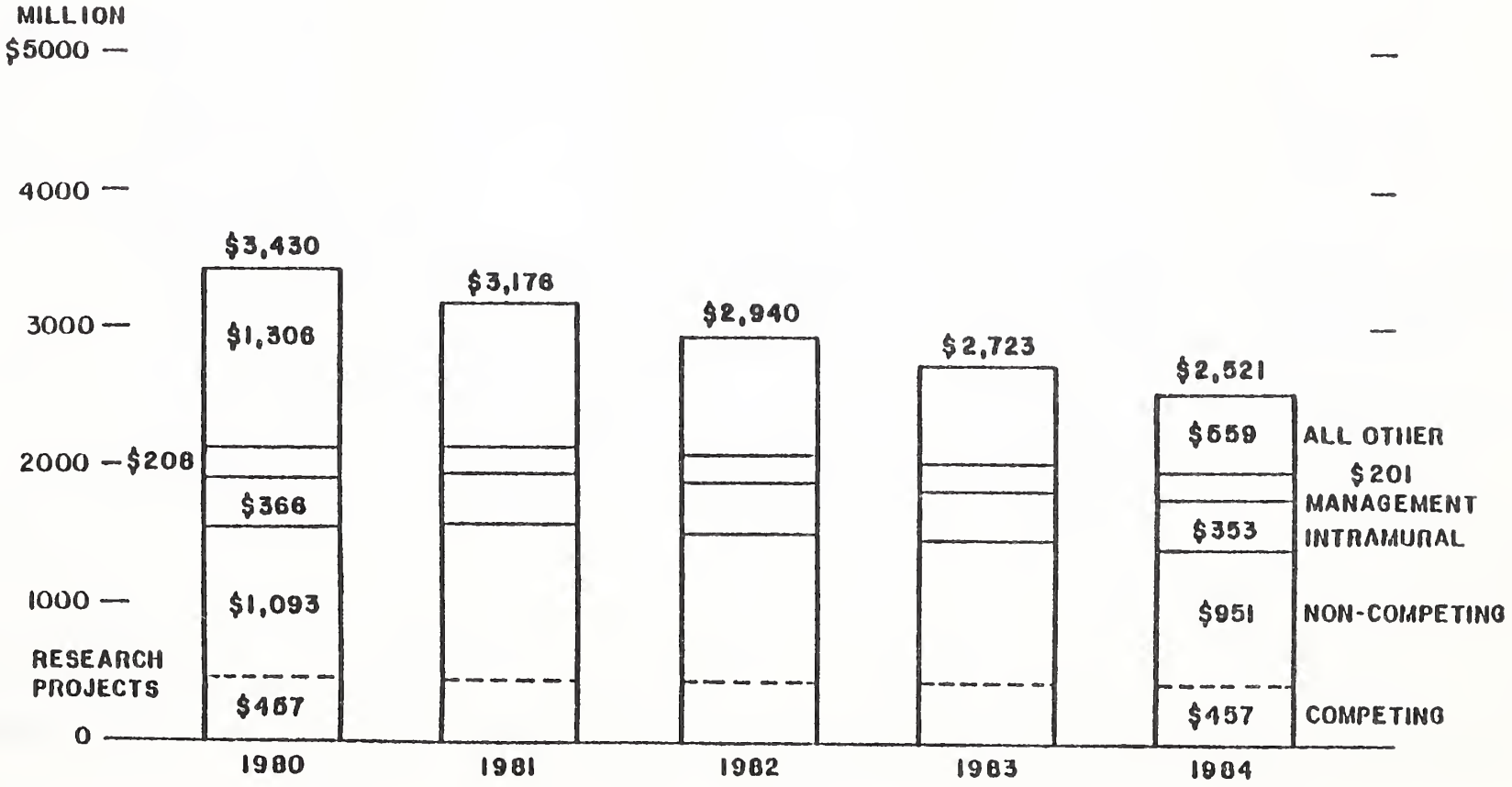


NOTE: 8% INFLATION ASSUMED FOR COMPETING RESEARCH PROJECTS AND COMMITMENTS MADE FY 1980 AND LATER.

Chart 6

TOTAL NIH FUNDS, FISCAL YEARS 1980-1984

CONDITION 2, IN CONSTANT FY 1980 DOLLARS



APPENDIX F

PLANNING AND EVALUATION OFFICERS'
AGENDA COMMITTEE REPORT ON THE NIH DIRECTOR'S
PLANNING AND EVALUATION REVIEW SESSIONS

Memorandum from the Associate Director for Program Planning and Evaluation to P&E Officers' Agenda Committee: The P&E Officers' Meeting (Feb. 25, 1980) 298

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MEMORANDUM

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH

TO : Chairman
Planning and Evaluation Officers
Agenda Committee

DATE: February 25, 1980

FROM : Associate Director for
Program Planning and Evaluation

SUBJECT: The Planning and Evaluation Officers Meeting

At the February 20 meeting of Planning and Evaluation Officers, I found discussions on the Director's program reviews and the development of the DRR program plan most interesting and useful. Perhaps it would be possible for the Agenda Committee to examine the Director's current program review process and to recommend improvements. I would welcome this.

With respect to the program reviews, a number of issues were raised that the Agenda Committee might wish to consider. These include:

- The need for a followup mechanism for Institute and OD critiques of the individual reviews.

- The need to define and further develop useful participation in the program reviews by Advisory Council members and by members of the Director's Advisory Committee. (It was noted at the meeting that the DAC only recently has begun to evolve into a policy planning group for all of NIH, and extensive briefing on particular program issues is required if individual DAC members are to contribute usefully to discussions.)

- The need for better definition of specific meeting purposes. While the meetings generally serve a variety of purposes--preparation for upcoming appropriations hearings, discussion of research plan priorities for next year's President's budget, examination of research plans themselves, etc.--can a sharper focus be provided on what the Director hopes to accomplish, to facilitate Institute preparation?

- The possibility of another review, or series of reviews, to consider planning and/or budget implications of matters raised in the appropriations hearings.

At the meeting I noted that these structured reviews initially dealt largely with description and analysis of the NIH mission in terms of the SATT framework. However, this past fall the research plan review had a specific budget-planning component, namely, stabilization of the science base, by supporting at least a specified member of traditional research grants and program projects grants. Over the next two years, this component will have to be expanded to include possibilities of stabilizing research environments

(especially research intensive institutions), both extramural and intramural. A meeting of the Director's Advisory Committee in May will be devoted to this issue. Clearly, this will be the major item in next fall's program reviews, and we need to consider how best to handle it to serve our various needs.

Please let me know your views. Thanks very much.

Joseph G. Perpich, M.D., J.D.

cc:
Members of the Agenda Committee
Mr. Carson
Dr. Schneyer

Planning and Evaluation Agenda Committee

Chairman

Dr. Jay Moskowitz
31/5A-03 (Heart Institute)

Mr. James Hill
31/2A10A (Child Health Institute)

Mr. Lou Carrese
31/11A49 (Cancer Institute)

Mr. Kurt Habel
1/205

Ms. Nancy Braymer
1/205

MEMORANDUM

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH

TO : Associate Director for Program Planning and Evaluation, NIH

DATE: August 12, 1980

FROM : Planning and Evaluation Officers' Agenda Committee

SUBJECT: Proposed Change in Director's Review Sessions

Attached for your review are the Agenda Committee's recommendations on how the Director's Research and Evaluation Plan Review Sessions could be improved and modified. The approach adopted by the Agenda Committee in developing these proposals has been to involve BID planning and evaluation staff at every stage and to ensure that the views and perspectives of all BIDs were solicited and considered, as follows:

- In May, the Agenda Committee held a series of meetings with BID planning and evaluation staff to elicit their ideas and concerns. A draft summary of the results of the meetings was prepared and sent to BID participants for review. The final summary, incorporating BID changes, is attached to this proposal.

- The Agenda Committee then developed a draft proposal based on BID concerns and suggestions expressed during the meetings. This proposal was sent to BID planning and budget officers for review with the suggestion that it be shared with BID Directors.

- The Agenda Committee held a meeting of the Planning and Evaluation Officers on August 8 to present and discuss the proposal. In general, the BID participants concurred with the thrust of the Committee's proposals and unanimously recommended that the proposal be officially transmitted to you. Many of the questions raised during the meeting dealt with the implementation of the proposals, specifically relationships among the planning, evaluation, and budget processes as well as scheduling and BID workload considerations. It was agreed that how these proposals would be implemented should be further delineated and subsequently presented to BID Planning and Evaluation Officers.

The Agenda Committee further recommends that this proposal be discussed at a BID Directors' meeting.

Jay Moskowitz, NHLBI, Chairman

Kurt Habel, OD

Nancy Braymer, OD

James G. Hill, NICHD

Louis Carrese, NCI

H. Richard Miller, OD

Helen Gee, OD

Solomon Schneyer, OD

Attachments

cc:
BID Planning and Evaluation Officers
BID Budget Officers

August 12, 1980

PROPOSED CHANGE IN DIRECTOR'S REVIEW SESSIONS

Background

In February 1980, the Associate Director for Program Planning and Evaluation, NIH asked the Agenda Committee of the BID Planning and Evaluation Officers to examine the annual Director's review sessions and to recommend improvements. The Agenda Committee subsequently met with principal planning and evaluation staff from each BID to elicit their suggestions on how both the Director's Research and Evaluation Plan Review Sessions might be modified to derive maximum mutual benefit from these structured interactions between the OD and the Institutes. Although each Institute was pleased with these interactions, there were a series of concerns expressed.

Major Concerns

The major concerns expressed by the BIDs about the review sessions may be summarized as follows:

1. Objectives:

   - The purposes served by the review sessions are not clearly defined. In one form or another, without consistency or predictability, a variety of different purposes seem to be pursued through the research plan review sessions: (1) briefing the Director, NIH, for the Appropriation Hearings; (2) discussion of issues or problems facing an Institute; (3) discussion of policy changes proposed by the Director, NIH; (4) presentation of selected aspects of an Institute's program activities; (5) discussion of fiscal and program plans for the upcoming two fiscal years; (6) development of a budget ceiling for the planning year; and (7) discussion of certain program changes. While the purpose of the Evaluation Plan Review Sessions is more specific, the conduct of the meetings has tended to involve a departure from focusing on those major issues and program activities meriting consideration for evaluation. The purposes of these sessions should be clarified.

   - In pursuing multiple purposes simultaneously, several important needs are not consistently met. Agenda items are not always covered; the research plan submissions are only peripherally discussed; issues of concern to the BIDs do not always receive the in-depth consideration they merit; discussion of long-range plans is sometimes diverted by attention to more immediate issues; and the type of decisions or feedback required concerning BID proposals or plans often is not provided.

- Planning and evaluation considerations, for the most part, are not separated in the Institutes and could be usefully combined in a single review session. Only one Institute that commented on this aspect of the review sessions advocated retaining separate meetings.

- The written material provided in advance of the review sessions (the BID research and evaluation plan submissions) is rarely discussed at or used during the review sessions. Materials prepared should have direct relevance to items discussed at the review sessions.

2. Budget:

- There was strong support for continuing with the effort to further align and relate the planning and budget processes. The way in which these functions are structured should reflect the planning and evaluation/budget continuum through which program progress is assessed, research opportunities identified, research strategies and plans formulated, budget requirements identified, and resource allocations made.

- The amount of budget data required in preparation for the review sessions was viewed as excessive in terms of the purposes served by the reviews. Every effort should be made to hold this material to a minimum.

3. Participants:

- The participation by Institute Advisory Council members in the review sessions was generally perceived as useful, while the nature of the participation by the Director's Advisory Committee members was less clear. If this participation is to be continued, a better defined and more structured role for external advisors in these sessions should be considered. Advance preparation and orientation of DAC and Council members is considered essential to their participation in the sessions.

- Opinion was divided on the question of attendance at the session. Several BIDs viewed the large number of attendees as a deterrent to a frank exchange of views; others favored the broadest possible participation by OD and Institute staff. A related concern involved the need for greater interaction between OD and BID staff prior to, during, and following the sessions.

Highlights of the comments and suggestions made by BID planning and evaluation staff are contained in the attachment.

Proposed Changes

The Agenda Committee recommends that the two review sessions held each year between the Director, NIH, and the Institute Directors be retained, but that the purpose of these sessions be redefined and the meetings be restructured, as follows:

- Planning/Appropriation Briefing Sessions (December - January)

1. Purpose--The purpose of this session would be to brief the Director, NIH, for the Appropriation Hearings (FY 1982) and to provide the information and justification needed by the Director to subsequently establish tentative budget ceilings for the Institutes (FY 1983). The Appropriation Hearings are usually held in February and other planning/budget documents (e.g., the NIH contribution to the PHS Three-Year Strategy Plan which requires a 1983 NIH budget level) are usually due about the same time.

2. Timing--These review sessions would be held in December and January and would be scheduled from 45 minutes up to one and one-half hours.

3. Participants--The BIDs which receive an appropriation would participate: the research Institutes, DRR, FIC, and NLM. Briefing sessions would be held with the other service components (CC, DRS, DCRT, DRG, Office of Research Services) if mutually agreed upon by the Director, NIH, and the BID Director. The coordinating committees for the trans-NIH health problems would be asked to submit a brief statement of issues which might arise at the Appropriation Hearings. The Director, NIH, would then decide if a review session were necessary.

4. Attendance--Both OD and BID attendance would be limited. OD participants would include the Director, NIH, the Deputy Director, Deputy Director for Science, Associate Director for Extramural Research and Training, Associate Director for Program Planning and Evaluation, the OD initial reviewer, OD planning, evaluation and financial management staff, and others at the discretion of the Director. The BID director would invite those senior support staff members he or she deemed appropriate.

5. Scope of Session--The following agenda would be covered:

   -- Present Fiscal Year (e.g., 1981): Several examples of areas of research holding great promise for progress and/or major advances and recent accomplishments.

   -- Next Fiscal Year (e.g., 1982): Institute priorities and major program changes in the context of the FY 1982 budget process--the major focus of the session in preparation for the Appropriation Hearings.

-- Future Fiscal Year (e.g., 1983): Description and rationale for major program changes planned--directed to summary information and justification needed by the Director in subsequently establishing a tentative FY 1983 budget ceiling. The rationale for planned program changes should emphasize evaluation studies where appropriate.

-- Issues: Discussion of Institute needs for resources and personnel and any issues anticipated to arise at the Appropriation Hearings.

(In the case of those service components and trans-NIH coordinating committees for which a planning/appropriation briefing session were determined to be beneficial, the meeting would primarily focus on the issues identified that may arise at the Hearings.)

6. Documentation--Material submitted in advance of the sessions should be held to a minimum and be directly relevant to the agenda for the session which will be patterned after the four major elements described under item 5 above. The Institute submissions, for which explicit guidance will be developed, can also form the core of the BID research plan submissions which would then be modified after the sessions and included in the NIH Research Plan to be prepared in early spring. Abbreviated summaries of the meeting highlights emphasizing follow-up actions would be prepared and shared with OD staff and other BIDs.

7. Rationale--Underlying this proposed change is the perception that a mutual briefing for the Appropriations Hearings is both necessary and desirable; however, inclusion of this objective within the context of the research plan review session has served to divert necessary attention from longer range issues and concerns. This proposal retains the alignment of planning, evaluation and budget processes and should provide a structure through which priorities and problems can be freely discussed.

- Program Review Sessions (Spring - Fall)

1. Purpose--These review sessions would provide the Director, NIH, and the Institute Directors an opportunity to consider and explore program and policy issues of mutual interest, including: major NIH policy changes and their implications (e.g. stabilization initiative); issues or problems facing a BID: long-range program developments and initiatives; reviews of research areas; and planning and evaluation activities. These sessions would not be tied to any specific budget event, would combine both planning and evaluation concerns without being tied directly to the development of the research or evaluation plan, and would provide a forum for the discussion of science as well as management problems.

2. Timing--These review sessions would begin in the spring and extend through the fall, and would be scheduled for one to two hours. The sessions would be divided into two groups: the meetings with the research Institutes would be held from March through July; those with NLM, FIC, service organizations, and trans-NIH coordinating committees (as applicable) would be held from September through November.

3. Participants--All Institutes would participate, as well as DRR, DRS, DCRT, DRG, CC, NLM, FIC, and Office of Research Services. The trans-NIH coordinating committees would be asked whether a review session would be beneficial and, if so, requested to submit a brief statement of the issues to be raised. The Director, NIH, would then decide if a review session should be held.

4. Attendance--Attendance would not be limited and would include the Director, NIH, OD staff and supporting staff, Institute Director, Institute program and supporting staff. Institute Advisory Council members and members of the Director's Advisory Committee would be invited to participate in these sessions.

5. Scope of Session--The scope of each session would depend upon the policy concerns that particular year that the Director, NIH, would like to explore and the items that the BID Directors wanted to raise. The agenda would be developed in advance by mutual agreement between OD and the Institute.

6. Documentation--Material submitted in advance should be limited and tailored to the agenda. A follow-up memo summarizing the discussion and the understandings reached would be prepared and widely circulated.

7. Rationale--This proposed change is intended to provide a context through which many of the needs identified by the BIDs could be met. It also would provide a forum for the Director, NIH to share his proposals and explore their implications with the BIDs and representatives of the NIH constituency. The consolidation of the planning and evaluation sessions reflects the way in which these functions are structured in most of the BIDs. A primary consideration in recommending modifications to the central NIH processes has been to promote and support BID efforts to strengthen their individual planning and evaluation processes. Under this proposal, the evaluation plan can still be prepared in spring and early summer.

ATTACHMENT

Highlights of BID Comments on the Director's Review Sessions

The results of the meetings held by the Agenda Committee to elicit BID suggestions on how both the Director's Research and Evaluation Plan Review Sessions might be improved are summarized below. All of the BIDs that participated in the sessions were provided an opportunity to share their ideas and concerns. Comments of the three BIDs (NHLBI, NCI, NICHD) represented on the Agenda Committee are not specified but are reflected in the proposal for modification of the sessions.

DRR--Represented by Martin Blumsack and Alan Moore

(1) General Impressions and Concerns:

- The review sessions are expected to serve too many different purposes. However, the sessions seem to respond to the needs of the Director, NIH.

- DRR endorses involving advisory council members in the research plan review session; however, the Director should ensure that they have an opportunity to participate fully.

(2) Suggestions for Improvements:

- Additional mechanisms should be developed to supplement the review sessions. There should be additional meetings between BID and senior OD staff to consider major issues and problems including a meeting before the research plan review session to discuss the submission and legislative and budget proposals as well as a debriefing and feedback meeting after the session with the OD initial reviewer and other staff.

- Informal communications between OD and BID staff should be improved especially with respect to preparation for and follow-up to the review sessions.

NIGMS--Represented by Leo von Euler and Vivian Dickson

(1) General Impressions and Concerns:

- In general, the Institute is satisfied with the current structure of the review sessions. (By mutual agreement between OD and the Institute, a review session to consider NIGMS evaluation activities was not held this year.) The NIGMS program plans do not change significantly in their broad outlines from year to year, and it is appropriate that the research plan review session focus on planned changes and program redirections rather than the totality of an Institute's activities. The time allotted for the meeting is sufficient. NIGMS has experienced no difficulty in obtaining access to senior OD staff to discuss issues or concerns outside the context of the review sessions.

- NIGMS views the inclusion of members of the NIGMS advisory council and the Director's Advisory Committee as a positive development. The presence of NIGMS council members strengthened the Institute's presentation and served to ensure that agenda items of concern to the Institute were discussed. The NIGMS endorsement included a caveat involving the need for selectivity in asking external advisors to participate in the planning process.

(2) Suggestions for Improvements:

- While not offering any specific suggestions for improvement, NIGMS urged that any modifications proposed incorporate sufficient flexibility to accommodate differing BID objectives and needs.

NIAMDD--Represented by Carol Feld, Gladys Hirschman, and Gail Jacoby (Comments supplemented by a follow-up memo.)

(1) General Impressions and Concerns:

- NIAMDD favors maintaining the review sessions in their current format. The system works well and generates worthwhile activities within the Institute in preparation for the reviews as well as constructive interchange between OD and the Institute.

- The planning and evaluation sessions should continue to be held separately so that evaluation activities are not overshadowed by other issues.

- NIAMDD expressed concern about the adequacy of information and feedback provided by OD with respect to the anticipated content of the research plan review session, the Institute's plan submissions, and the views and information presented at the sessions.

(2) Suggestions for Improvements:

- Informal feedback from OD staff attendees would be helpful as a means of supplementing the necessarily formal memoranda which have been serving as follow-up to the meetings.

- Institute staff would also benefit from fuller briefing by OD staff, preferably in writing, on the priority and policy considerations to be discussed at the research plan review session.

- It would be useful if BID planning staffs could share their experience and ideas on techniques that have worked well in presenting program plans and briefing the Director.

- Encouraging budget staff's active participation in the review session could lead to greater integration of planning and budgetary activities.

- There is a need to clarify the role of advisory council members in the research plan review session and expectations associated with their participation.

NINCDS--Represented by Malcolm Ray

(1) General Impressions and Concerns:

- Underlying the concerns raised by NINCDS is the absence of a common understanding of the objective of the review sessions. A variety of different purposes seem to be pursued simultaneously; as a result, none of these are adequately met. Specific problems identified are (a) the agenda items suggested by the Institute were not discussed; (b) the research plan submission was only peripherally addressed; (c) there was little opportunity to discuss research programs as distinct from mechanisms of support; and (d) the relationship between the planning and budget processes is unclear as is the roles of the respective OD offices responsible for these functions.

- The number of staff attending the sessions inhibits a frank exchange of views.

- The members of the NINCDS advisory council who attended the research plan review session were pleased to have had the opportunity to participate.

(2) Suggestions for Improvements:

- The purpose of the review sessions should be clarified and then a framework devised conducive to meeting this objective.

- There should be an opportunity to discuss with the Director, NIH an Institute's substantive research plans and programs.

- Proposed changes in the review sessions should be considered and discussed by the BID Directors.

NIA--Represented by Don Gibson and Charles Wadkins

(1) General Impressions and Concerns:

- NIA views the research plan review session as the culmination of the internal Institute planning process, as preparation for the Appropriation Hearings and as an opportunity to elicit the Director's reaction on major issues and program directions. While the Institute has a clear sense of the purposes served by the sessions, there is a need to improve the "feedback" on key issues identified by the Institute. Not all of the agenda items were covered at the meeting, and there was no opportunity for staff interchange to clarify questions raised by the OD staff review of the Institute's research plan submission.

- It is important that the budgeting and planning processes be related.

- Participation by advisory council members contributed to the meeting and is viewed in a positive light.

(2) Suggestions for Improvements:

- Planning and evalution issues should be considered at the same review session.

- Provision should be made for interaction between OD and Institute staff at the session or other mechanisms developed to ensure that issues raised are clarified and resolved.

DCRT--Represented by L. Manuel and Michael Reed

(1) General Impressions and Concerns:

- In some respects, it is difficult for DCRT to engage in long-range planning as changes in the Division's activities are dependent upon external industrial innovation and developments. DCRT has no full-time planning staff, and the Division's planning procedures are highly centralized involving the Director and his senior staff.

- DCRT uses the review session to present information on the Division's activities and to convey accomplishments. The planning process, as currently structured, is appropriate for this purpose. Although the Division has elected not to use the research plan review session as a forum to discuss all major issues, preparation for the meeting serves to stimulate internal discussion and consideration of future program directions.

- From the Division's perspective, there is not a need for formal follow-up sessions to the review as this can occur through budget channels where warranted.

(2) Suggestions for Improvements:

- The number of OD staff present creates an imbalance and may act to hinder a frank interchange of views. The possibility of reducing the number of attendees should be considered.

DRG--Represented by Joan Porter

(1) General Impressions and Concerns:

- This was the first year that DRG participated in the formal planning process, and, in general, the Division was pleased with the experience. The meeting focussed on problems and opportunities facing the Division and resource requirements to address these. DRG intends to judge the effectiveness of the meeting by the outcome -- how the issues and needs identified are addressed.

- A substantial amount of effort was devoted to structuring the meeting and developing the agenda, and DRG provided a briefing book to aid in the discussion. Initial follow-up to the session was satisfactory and involved an identification of action items at the staff level.

- The large number of attendees did not pose any difficulties.

CC:--Represented by Howard Kettl and Steve Galen

(1) General Impressions and Concerns:

- The planning process has improved over time; in part, this is attributable to the Director's personal interest in the process, better preparatory and follow-up documentation, and the attempt to better integrate the planning and budget functions. This latter aspect brings discipline to the planning process and could be further tightened and restructured to more closely tailor consideration of program plans to the budget cycle.

- Preparation for the review session is useful in providing a structured context for internal decision-making and in formulating future CC directions.

- The research plan review sessions should continue to include discussion of legislative proposals and issues, as warranted.

(2) Suggestions for Improvements:

- Discussion of program plans at the review session should be structured around the three year budget cycle: (a) the current fiscal year in terms of accountability and ongoing programs; (b) the next fiscal year to prepare for the Appropriation Hearings; and (c) the planning year to consider future directions. Projections for the out-years should continue to be based on extrapolations and not be addressed in the discussion.

NEI--Represented by Julian Morris and Ed McManus

(1) General Impressions and Concerns:

- The NEI's overall experience with the review sessions has been positive with improvements noted as the process has evolved over time. The meetings provide a good forum for a productive interchange between OD and the Institute in general, and between the Director, NEI and the Director, NIH in particular. NEI attributes much of the success of the meetings to advance preparation and orientation of staff and to the Institute's structured planning process which feeds into the central NIH process.

- With the exception of the format for the research plan submission, NEI had no major problems with this year's research plan review session. The agenda was followed; the OD comments and follow-up review memorandum were satisfactory; and the discussion focussed on major issues and initiatives with an opportunity provided to discuss the substance of NEI programs.

- Despite initial reservations concerning the purpose and expectations for advisory council member participation in the research plan review session, this innovation proved to be useful, and the reactions of participating council members were uniformly positive. NEI staff invested considerable effort in briefing council members for the session; this orientation is believed to have contributed significantly to the constructive nature of the council members' participation.

- The presence of Institute program staff at the sessions is considered both important and desirable, and a concerted effort is made to encourage the broadest possible participation by program officials in the process.

(2) Suggestions for Improvements:

- Evaluation is an integral component of NEI planning activities, and the planning and evaluation review sessions should be combined into a single session.

- A major factor in improving the central NIH process would be to strengthen the "front-end" -- to improve BID planning and evaluation activities.

- The format for the research plan submission should be revised to highlight major issues and initiatives so that the written documentation more closely reflects the review session orientation.

- Every effort should be made to simplify the budget submission and to reduce the level of detail required.

NIDR--Represented by Jack Patterson and Dushanka Kleinman

(1) General Impressions and Concerns:

- The major purpose served by the NIDR research plan review session was to brief the Director for the Appropriation Hearings. While the meeting was useful from this perspective, there was not an opportunity to discuss long-range issues or plans, and the written submission was not relevant to the discussion.

- The participation by NIDR council members went well, and their reaction was favorable.

- The integration of budget data and program plans in the research plan submission is important and should be retained particularly as the research plan provides one of the few opportunities to present "professional judgment" estimates and initiatives during the budget cycle.

- The NIDR evaluation plan review session included a detailed discussion of recommendations resulting from an evaluation study conducted under contract. NIDR disposition of the recommendations made would have been more appropriately discussed in a different forum with limited attendance. The number of support staff who now attend the sessions tends to inhibit a frank interchange of views.

(2) Suggestions for Improvements:

- "One on one" meetings between the Director, NIH and a BID Director might provide a better forum to consider possible actions and priorities, particularly with respect to evaluation activities.

NIEHS--Represented by George Kingman and Billie Hudson

(1) General Impressions and Concerns:

- The review sessions have improved over time and are undertaken in a cooperative spirit between OD and the Institute. The base of experience and knowledge of the Institute's programs that has been built up over the years aids in focusing the discussion on specific issues and preparing for the Appropriation Hearings. The agenda for this year's research plan review session was scrupulously followed.

- In suggesting modifications to the review sessions, it is necessary to recognize certain realities. The symbolic value of the meetings -- in terms of being able to demonstrate a structured process for decision-making and review -- may outweigh the sessions utility as a forum to consider and discuss substantive program plans. Further, the level of interest and detailed knowledge of the Institute's research and evaluation plans demonstrated by the OD participants in the sessions varies based on differing functions and areas of responsibility.

- Despite initial reservations concerning the participation of advisory council members in the research plan review session, the involvement of an NIEHS advisor proved useful and contributed to the discussion.

- NIEHS favors wide attendance by both Institute and OD staff. This is helpful in future staff-to-staff interactions and serves to broaden the understanding of NIEHS programs.

- The Institute would like to retain the current scheduling of the research plan review session near the end of the calendar year as this timing has proved advantageous in preparing for other PHS and Departmental reviews.

- The integration of planning and budget submissions is valuable and should be retained. The budget data required seems excessive although an effort was made to reduce the number of tables this year.

(2) Suggestions for Improvements:

- The planning and evaluation meetings should be consolidated.

NLM--Represented by William Cooper and Susan Buyer

(1) General Impressions and Concerns:

- The expectations and objectives of the review sessions are not clear.
- As a largely service oriented bureau, NLM has experienced difficulty in applying NIH-wide concepts and policies (e.g. the SATT methodology) tailored to research activities to NLM program operations. In recommending changes to the current review session structure, it is important that adequate consideration be given to the special nature and requirements of the NIH service components.
- Differing requirements imposed by central OD budget, research plan, and evaluation processes have resulted in some duplication of effort at the BID level, and the possibility of more closely integrating these functions should be explored.
- The participation of NLM Board members in the research plan review session was extremely helpful and may lead to a more formalized role for the Board in the Bureau's planning activities.
- Preparation for the sessions provides a valuable stimulus and context for internal discussions and decision-making.
- Wide attendance by OD and NLM staff at the sessions is a positive feature and serves a useful educational function.

(2) Suggestions for Improvements:

- The planning and evaluation review sessions should be combined into one meeting.
- Interaction between OD and NLM planning staff should be increased both in terms of preparation and follow-up activities.

MEMORANDUM

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH

TO Chairman
Planning and Evaluation Officers'
Agenda Committee

DATE: August 18, 1980

FROM Associate Director for
Program Planning and Evaluation

SUBJECT: The Agenda Committee's Report on the NIH Director's Planning and Evaluation Review Sessions

I am writing to acknowledge your memorandum of August 12 transmitting the Agenda Committee's recommendations on how the Director's Research and Evaluation Plan Review Sessions could be improved and modified. I was very much impressed with the report and the recommendations.

As you know, your report was a result of the February 20 meeting of Planning and Evaluation Officers which focused on the Director's program reviews. As a result of that meeting, I requested your Committee to examine the Director's current program review process and to recommend improvements (see Attachment A). I intend to review the report thoroughly with Bruce Carson, Sol Schneyer, and OPPE staff, and, in view of the recommendations on the Planning/Appropriation Reviews, I also plan to discuss it with Cal Baldwin, Associate Director of Administration. Subsequently, the report will be reviewed at a future OD Staff and Institute Directors' meeting. It is my intention to keep a careful record of all comments on the recommendations and their implementation.

I was most impressed with the recommendations on the nature of the suggested reviews with Dr. Fredrickson. In large part these conform with my own assessment of what we need in Phase III of the NIH planning and evaluation process. (Phase I covers the planning reviews and Phase II the evaluation reviews.) I was also impressed by the pains you and your Committee have taken to ensure the broadest participation of the Institutes in this effort.

In my view, the current Planning and Evaluation Reviews are of as much value to the Institutes as they are to the Director, NIH. They ensure a well-coordinated and consistent NIH approach in presentations before the Appropriations Committees and in the preparation of the President's budget. The emphasis on separate reviews for evaluation was prompted by the perception that the evaluation process needed far more attention from the Director, NIH, as well as the Institute Directors. However, your recommendation concerning the inclusion of evaluation issues in the spring and summer program reviews seems eminently sound.

In sum, you and your Committee and all of the Planning and Evaluation Officers are to be commended for this candid and useful assessment of

our current planning and evaluation processes and of means to improve them. I intend to move expeditiously with our reviews so that these recommendations can be implemented, where appropriate, at the beginning of the next fiscal year. You and your Committee will be invited to participate in the discussions when these matters are taken up at the OD Staff and BID meetings.

Thank you very much.

Joseph G. Perpich, M.D., J.D.

Attachment A

cc:
Planning and Evaluation Officers'
Agenda Committee

MEMORANDUM

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH

TO : Director, NIH

DATE: September 8, 1980

FROM : Associate Director for
Program Planning and Evalution

SUBJECT: OD Staff Meeting Review of the Report on the NIH Director's Planning and Evaluation Review Sessions

The OD Staff Meeting of September 4 was devoted to a review of the report of the Planning and Evaluation Officers' Committee relating to proposed changes in the NIH Director's Planning and Evaluation Review Sessions. Following is a summary of the discussions.

I began by briefly reviewing the genesis of the Committee report. I noted that I meet once a month with Planning and Evaluation Officers to review issues of mutual concern. At the February 1980 meeting of that group, we discussed proposed changes in the Director's Program Review Sessions. As a result of that meeting, I requested that the Agenda Committee, chaired by Jay Moskowitz, Associate Director for Program Planning and Evaluation, NHLBI, examine the Director's current program review processes and recommend improvements. Dr. Moskowitz and his Committee undertook a thorough review and transmitted a report to me on August 12. Subsequently, I discussed the report's findings and recommendations with Sol Schneyer and his Division of Program Analysis staff, and also with Cal Baldwin (for possible implications with respect to ADA.) We agreed that the report should be reviewed by OD staff; hence, the purpose of this meeting.

Dr. Moskowitz briefly summarized the process by which the Committee developed the report and reviewed the report's recommendations. He indicated that his Committee initially held a series of meetings with BID Planning and Evaluation Staff to hear their ideas and concerns. The Committee then prepared a draft summarizing those meetings, which was subsequently reviewed by all BID staff. On the basis of BID recommendations, the Committee developed a proposal that was extensively reviewed by Institute staff and ultimately transmitted to me for action.

Dr. Moskowitz then summarized the report's recommendations. One recommendation is that there be two series of review sessions with the NIH Director each year. The first, planning/appropriation briefing sessions, would be held in December and January. In addition to briefing the NIH Director for the appropriation hearings, these sessions would provide Institute budget ceilings for succeeding fiscal years. It is the intent that the sessions would deal with science and budget issues not only for the present fiscal year, but for the succeeding year and beyond. Personnel and other resource needs and anticipated appropriation hearing issues would also be addressed.

Dr. Moskowitz noted that the second series of review sessions would be scheduled in the spring and fall. Here, the BID Directors would consider with the NIH Director program and policy changes of mutual interest. There would be broad BID and OD representation at these meetings, and members of Institute Advisory Councils and of the Advisory Committee to the Director, NIH, would be invited to attend.

I noted as a followup to Dr. Moskowitz's presentation that I have already asked Sol Schneyer and his staff to examine (1) implications of the report for the development of NIH planning documents, (2) the role of the DAC members in the spring reviews, and (3) how evaluation reviews could be incorporated into the program review process in the spring and summer.

You observed that the proposed changes for the planning/appropriations briefing sessions in the fall are appropriate and provide a better focus for the upcoming hearings. However, you noted that as important, or even more so, are the needs for review sessions in preparing the NIH budget for presentation to the Surgeon General and the Secretary. You said that in the past much of the NIH attention has been devoted to preparations for the appropriations hearings without a similar emphasis in regard to Department budget reviews. However, with increasing fiscal constraints, budgetary decisions in the Department leading to the President's budget are becoming increasingly important. And here it is essential that NIH be better prepared to speak in a collective voice. You noted that there is increasing convergence of the planning and budgeting processes and that this must continue. We can no longer afford separate processes; a need exists for a more collective approach in dealing with the major program and budgeting issues of the NIH vis-a-vis the PHS, the Department, OMB, and the Congress.

Dick Miller noted that the budget processes within the Department begin in April with submission of the NIH preliminary budget to the PHS by May 1 and the presentation to the Secretary in June and July. You indicated that you and future Directors of NIH must be as well prepared for the Departmental budget reviews as for the Congressional appropriations hearings. Henceforth, there will be less competition for funds among the Institutes and probably more competition between NIH as a whole and other agencies within the Department. In this regard, Dr. Moskowitz said that these reviews will serve not only as the basis for appropriations hearings, but also in part for the Departmental budget reviews.

You felt that there were two imperatives here. The first was that the Director, NIH, must be fully informed in regard to Institute programs and budget needs. The second was that the NIH Institutes together must understand the major program policy and budget issues and how to reach some consensus or collective agreement on them. I said that this, indeed, was what the two reviews were attempting to achieve. The first series is designed to inform the NIH Director and individual Institute Directors for purposes of the appropriations hearings and budget reviews in the next fiscal year. The purpose of the second series is to address collective problems by means of an agenda that could be developed among OD Staff and the Institutes on key policy issues of succeeding fiscal years.

Dr. Goldberger questioned the limited participation in the planning appropriation reviews, as did Cal Baldwin. In response, Dr. Moskowitz and Lou Carrese said that Scientific Directors certainly could participate. However, the thrust of these reviews was to deal with the key budget issues for the appropriations hearings. General program issues would be the focus of the second series of reviews.

There was general agreement that the recommendations of the report were sound and that they should be reviewed by the Institute Directors. It is clear that over the next year more work will have to be done on the guidances for the two review sessions and their implementation. The issues that you raised in regard to the budget reviews will also need to be addressed by planning and budget officers in terms of the processes proposed. It may be that these may not be appropriate to the particular needs of the Department's budget cycle, and perhaps additional effort by Dr. Moskowitz and his Committee may be warranted. I will schedule further discussion of the Committee's report for the September 18 meeting of the BID Directors so that we can decide on appropriate followup actions.

Thanks very much.

Joseph G. Perpich, M.D., J.D.

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH

TO : BID Directors
OD Staff

DATE: October 2, 1980

FROM : Associate Director for
Program Planning and Evaluation

SUBJECT: BID Discussion of the Report of the NIH Director's Planning and Evaluation Review Sessions

Enclosed is the summary of the discussion at the BID Directors meeting of September 25 devoted to the report on the NIH Director's planning and evaluation review sessions. Sol Schneyer and his staff are developing guidances for the "Winter" meetings. These guidances incorporate the P&E Officers recommendations for restructuring the Director's Reviews.

During the year we will share with you the guidances and other relevant documents as they become available. Thanks very much.

Joseph G. Perpich, M.D., J.D.

Enclosure

cc: Planning and Evaluation Officers

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH

TO : Director, NIH

DATE: October 2, 1980

FROM : Associate Director for
Program Planning and Evaluation

SUBJECT: BID Discussion of the Report on the NIH Director's Planning and Evaluation Review Sessions

The BID meeting of Thursday, September 25, was devoted to a discussion of the report of the planning and evaluation officers' committee relating to proposed changes in the NIH Director's planning and evaluation review sessions. Tom Malone chaired in your absence. As you know, the report was reviewed at your OD staff meeting of September 8 (see Attachment 1).

I briefly summarized the genesis of the committee report and Jay Moskowitz reviewed the report's recommendations. Dr. Malone inquired whether the two series of sessions would not require too large a commitment of the Director's time and whether there was flexibility in terms of the number of reviews scheduled. I responded that indeed one of the reasons for examining the process was to determine the appropriate number of reviews. I pointed out that last fall's 25 reviews extended into the winter; these demonstrated the enormous amount of time and effort that was being invested by you, the Institutes and our respective staffs. Dr. Moskowitz pointed out that the recommendations do provide for flexibility regarding the number of sessions, especially with respect to the spring reviews. The spring reviews could cover a broader range of activities, depending upon the needs of the Institutes and the Director.

Dr. Bowery noted the difficulty in implementing the recommendations, at least for the forthcoming fall reviews. He noted that in the past those reviews have been primarily programmatic, for purposes of the Appropriations hearings; the report recommends that they be devoted to the Appropriations as well as to the proposed President's Budget for the next two fiscal years. It may be too difficult to try to address each of these budgetary cycles within the one review. He noted that the new approach places the fall reviews in a different context--one which has not obtained in the past. He also expressed concern about the time limit of 45 minutes to an hour-and-a-half for each session. Dr. Tower shared Dr. Bowery's concerns. In his view, the two review sessions seemed to make a distinction between budget issues on the one hand and program issues on the other. He said that inevitably there is overlap and that program issues will have to come up in the fall and budget issues in the spring reviews. And he felt that the proposals for the spring and fall reviews would change the nature of these sessions. Presently they comprise selected reviews on the basis of the evaluation plan. Now the recommendation is to broaden the reviews to go beyond evaluation and programmatic

issues. Clearly, implementation of the recommendations must be carefully considered by the Institutes and the Office of the Director, especially by the respective planning and budgeting staffs.

Dr. Moskowitz replied that Dr. Tower's and Dr. Bowery's concerns were addressed throughout the development of the committee report. He noted that in fact there has to be overlap in the sessions on program and budget. Indeed, the spring review should set the stage for the fall planning and budget reviews. Moreover, the fall reviews were not to be devoted exclusively to budget matters but to the underlying programs as well. The difficulties noted apply to this transition year; with next year's fall reviews the necessary preparatory work will have been done.

Dr. Bowery said that it would be most important to get out guidances as soon as possible for the reviews this fall. He said that the Institutes and their staffs should be fully informed on the nature of the reviews and on the changes from the previous practice. I said that Dr. Schneyer and his staff have the lead responsibility for developing the guidances and that they should be sent shortly to budget, planning, and evaluation officers for comment. Dr. Schneyer noted that the two reviews differ in relative emphasis. The fall reviews are for the shorter term issues and the spring for the longer term issues. He pointed out that the revised approach was experimental and that we may have to modify the reviews along the way. He observed that we will always have the problem of discussing program and budget in relation to upcoming Appropriations and the President's Budget.

Dr. Leventhal commended the work of Dr. Moskowitz and his committee for a very skillful effort in attempting to improve processes in a most difficult area. Essentially, the basis for all of these meetings is to promote communication and flow of information among the Institutes.and the Office of the Director, but he echoed concerns expressed by Dr. Krause of ensuring enough flexibility for presentations and discussions in the reviews. He pointed out, however, that the structure for the reviews, while important, should not be the only concern; the discussions were the important thing. Dr. Kirschstein agreed with Dr. Leventhal, noting that the last two reviews were the best; she hoped that the achievements of these reviews were not compromised by the report's recommendations.

Dr. Moskowitz responded that the recommendations were indeed responsive to the concerns raised by Drs. Leventhal and Kirschstein. As he pointed out at the recent OD staff meeting, the planning/appropriations reviews could be characterized as "required." These would be limited sessions addressed to key programmatic and budget issues for the Appropriations hearings for the next budget cycle. The spring and summer reviews might be termed "elective," with the agenda and the nature of the review directed toward program issues of concern to the Institutes and the Office of the Director. The latter sessions would involve more staff participation, as well as participation of Advisory Committee members. He observed that the whole thrust of the report's recommendations is to enhance planning and budgeting integration and to improve communication among the Institutes and the Office of the Director, as Dr. Leventhal had indicated. Dr. Tower asked whether the term "elective" referred to the agenda for the meeting or to the meeting itself. Dr. Moskowitz responded that the term could be applied to both.

Dr. Malone concluded by noting that the planning process instituted four years ago has slowly evolved into a most important forum for the Institute Directors and the Director of NIH. Clearly, the report's recommendations had considerable merit, and there seemed to be general agreement, both among OD staff and the Institute Directors, that the recommendations ought to be implemented. However, care must be taken that the enormous success of past program reviews not be compromised and that there be sufficient flexibility in terms of the structure and agenda for the meetings.

On the basis of the BID meeting, I have asked Dr. Schneyer to take the lead in developing the guidances for the planning of the reviews this fall. I have also asked him to undertake some preliminary work to address possible guidances for the spring and fall reviews and the issues raised about planning/budget coordination for you and the Institute Directors in regard to your preparation for the budget reviews within the Department. I have created an Evaluation Oversight Committee with a task force to be chaired by Dr. Edward Sondik, Chief, Program Analysis and Evaluation Branch, NHLBI, to consider how evaluation plans can be part of the spring and fall reviews. Dr. Schneyer will work very closely with Norman Mansfield and his staff and the relevant BID planning and evaluation and budget offices in considering these areas. The guidances for the planning and evaluation reviews are the first order of business. When these have been hammered out, they will be reviewed at future OD and BID meetings. This area will clearly be a continuing agenda item for OD staff and your Institute Directors meetings for the next fiscal year.

Thanks very much.

Joseph G. Perpich, M.D., J.D.

Attachment

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